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UNITED STATES DISTRICT COURT
WESTERN DISTRICT OF WISCONSIN

PROMEGA CORPORATION,

Plaintiff,

MAX-PLANCK-GESELLSCHAFT ZUR FORDERUNG DER WISSENSCHAFTEN E.V.,

Case No.: 10-CV-281

Involuntary Plaintiff,

v.

LIFE TECHNOLOGIES CORPORATION, INVITROGEN IP HOLDINGS, INC., and APPLIED BIOSYSTEMS, INC.,

Defendants.

EXPERT REPORT OF RANDALL DIMOND

The following information is provided pursuant to Rule 26(a)(2)(B):

1. A complete statement of all opinions to be expressed by me at trial and the basis and reasons for all such opinions is attached hereto as **Attachment 1**. I reserve the right to supplement this report, as appropriate, after reviewing any further information provided in the case.

2. The data and other information considered by me in forming the opinions noted in paragraph one are identified in Attachment 1.

3. A copy of my curriculum vitae, which includes my qualifications and a list of all publications authored by me is attached hereto as Attachment 2.

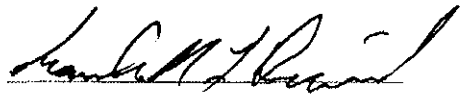
4. I am Vice-President and Chief Technical Officer of Promega Corporation ("Promega"). I hold a Bachelor of Science degree from the University of Utah and a Ph.D. degree from the University of California, San Diego. I am currently also an Adjunct Professor at the University of Wisconsin-Madison.

5. I have not provided any testimony in civil proceedings in the U.S.A. in the last four years.

6. I am not being compensated for this report beyond my normal salary.

7. Having been informed that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the U.S. Code, I declare under penalty of perjury that the following is true and correct.

Dated this 11th day of July, 2011.



Randall L. Dimond, Ph.D.

ATTACHMENT 1 TO EXPERT REPORT OF RANDALL DIMOND

If called to testify in this case, I will express the following opinions at trial, the basis and reasons for which are set forth below and detailed in the documentation identified below. I reserve the right to supplement these opinions in the event of new information.

1. In preparing this report, I reviewed the so-called Tautz Patent (RE37,984) as well as the Promega Patents, i.e. U.S. Patent Nos. 5,843,660 ('660); 6,221,598 ('598); 6,479,235 ('235); and 7,008,771 ('771). I am familiar with the technology utilized in these patents. The Promega Patents disclose and claim methods of simultaneously determining specified DNA markers in a human genome by methods that include multiplex PCR. The primary applications for these methods in the past have been in the fields of forensic analysis, DNA typing, and paternity determination. The nature of each of these fields is briefly discussed below.
2. In preparing this report, I reviewed numerous publications found in the scientific literature and on various company websites reporting on the use of STR technology in a variety of different scientific disciplines. A number of these publications are discussed in more detail below. However, there are additional publications of the same type that have been, and will continue to be, provided through discovery and I reserve the right to testify regarding them.

A. Nature of the Fields Applicable to Multiplex STR Analysis

3. For the reasons detailed below, it is my opinion that the use of STR multiplex kits in the following applications are not "Forensics and Human Identity" or "Paternity" applications: monitoring bone marrow transplant engraftment;

genotyping hydatidiform moles; cancer analysis; determination of fetal sex; archeological and anthropological research; clinical research on inherited genetic and acquired diseases; and confirming that cell cultures or cell lines are uncontaminated, correctly identified, and/or genetically unique (collectively cell line authentication).

4. A useful definition for Forensic Testing is found on the Human Identity Trade Association (HITA) website (http://humanidentity.org):

"Forensic DNA testing serves a number of useful purposes. It can be used to track down criminal suspects who have left behind biological evidence, exonerate individuals who have been falsely accused of committing crimes, identify individuals who have fallen victim to violent crimes or disasters, and connect crimes that share biological evidence. It can also be used to identify the father of a child conceived through rape or incest."

To summarize, forensic uses are legal in nature and include a) uses to inculpate perpetrators and exclude falsely accused individuals, b) uses to identify victims of a violent crime or mass fatality, or c) identify the father in a criminal paternity case.

5. Forensics involves human identity testing. The fundamental question for human identity testing is: who is this person? The process starts with a sample, the human source of which is unknown, and (if successful) proceeds to the identification of the human from which the sample is derived.

6. That clinical uses are distinct from forensic and paternity uses can be seen from the language of the Promega patents. For example, the '771 Patent notes that the

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technology has specific uses "in the field of forensic analysis, paternity determination, monitoring of bone marrow transplantation, linkage mapping, and detection of genetic diseases and cancers." ('771 Patent, col. 5, lines 50-53).

7. [redacted]

8. [redacted]

9. "DNA typing" is a more general term than Forensic or Paternity testing. DNA typing can involve the typing of tissue or cell cultures where the question is not: who is this person? For example, DNA typing by multiplex analysis of STR loci today is routinely done for research purposes and for clinical purposes, e.g. clinical diagnostic, treatment, and clinical research purposes. Clinical diagnostics

involves diagnostics in a clinical setting, e.g. a setting in which clinical diagnostic results influence patient treatment. Similarly, clinical research involves research in a clinical setting. It typically involves the use of human subjects or materials directly derived from human subjects. By contrast, research that is not done in a clinical setting typically does not involve living human subjects but encompasses a wide variety of experimental questions and subject material.

10. Starting in the mid-1990s, there has been a growing use of commercial STR kits for clinical purposes, including but not limited to monitoring bone marrow transplantation engraftment, genotyping hydatidiform moles, characterizing and diagnosing cancer, and contamination testing (including cell line authentication). See J. Pfeifer *et al.*, The Changing Spectrum of DNA-based Specimen Provenance Testing in Surgical Pathology, *Am. J. Clin. Path.*, 135:132 (2011) that utilized AmpFlSTR® Profiler Plus® (attached as Exhibit 1). All of these applications of STR multiplex analysis are distinct from forensic and paternity applications and are discussed in some detail in the sections below.

a. bone marrow engraftment monitoring

11. The monitoring of bone marrow transplants in human patients is done in a clinical setting, i.e. the transplant is done for the treatment of the patient. The fundamental question involved in monitoring transplant engraftment using STR multiplexing is not: who is this person? It is not for the purpose of human identity because, after all, the identity of the donor and recipient in the transplant is known. Rather, it is to monitor the engraftment of the transplant, i.e. whether the donor bone marrow cells are growing and contributing to the circulating blood

cells of the recipient. Any residual recipient circulating blood cells are also monitored for a variety of purposes including detection of recurrence of disease. Thus, this clinical field is clearly distinct from the forensic field.

12. Following bone marrow transplantation, the recipient may produce their own (host) cells as well as donor blood cells. This is called "chimerism," i.e. a mixture of cells originating from two individuals. Chimerism analysis provides quantitative information about the transplant and can serve as a prognostic factor. Commercial multiplex STR kits and their associated protocols are carefully designed so that the relative amount of amplified DNA for each STR allele is proportional to the amount of genomic DNA containing that allele in the sample being analyzed. Thus, comparing the amount of amplified STR alleles from donor versus host provides an indication of the proportion of blood cells contributed by each source. Repetitive testing over time provides an indication as to whether the proportion of blood cells from the donor and host are changing, which has treatment and prognostic value.

13. As noted in Liang et al., there are instances where "decisions to alter treatment are based on major shifts in the degree of chimerism . . .". Liang *et al.*, *J. Mol. Diag.* 10:142-6 (2008) at p. 145 (attached hereto as Exhibit 2). In some cases where analysis of chimerism indicates a relapse risk, relapse can be prevented by changing therapy, e.g. withdrawing immune suppression and/or by administering infusions of donor cells (such as donor lymphocytes). See Pulsipher *et al.*, *Biol. Blood Marrow Transplant*, 15:62-71 (2009) at p. 65 (attached as Exhibit 3).

14. Thus, in the clinical field of bone marrow transplantation, multiplex STR analysis to monitor bone marrow engraftment has become an important tool for the physician to increase the chances of transplant success in treating malignancies. While there are other tests that might be used, "the overwhelming majority of laboratories" continue to use STR multiplexing in this manner. Liang *et al.*, *J. Mol. Diag.* 10:142-6 (2008) at p. 142 (attached hereto as Exhibit 2) (see introduction). Liang *et al.* used the AmpFlSTR® Profiler® kit for monitoring of bone marrow engraftment.

15. Chimerism analysis is generally performed serially. The presence of recipient cells following transplantation (particularly a non-ablative transplant) may not indicate residual disease or relapse because normal/non-malignant recipient cells may be produced post-transplant. Therefore, serial analyses are performed to monitor for an increase in recipient cells, which is associated with the reappearance of the underlying disease. See Pulsipher *et al.*, *Biol. Blood Marrow Transplant*, 15:62-71 (2009) at p. 65 (attached as Exhibit 3).

16. The time interval between a change in chimerism and relapse can be very short. Therefore, serial analysis of chimerism by STR-PCR needs to be done frequently during the first 100 to 200 days after transplantation, when most relapses occur. See Pulsipher *et al.*, *Biol. Blood Marrow Transplant*, 15:62-71 (2009) at p. 66 (attached as Exhibit 3). Some groups emphasize repeated testing in the first month post-transplant followed by increased time periods between testing during the first year and annual testing thereafter. See Kristt *et al.*, Assessing Quantitative Chimerism Longitudinally, *Bone Marrow Transplant*, 39:255-68

(2007) at p. 266 (attached as Exhibit 4). Where other markers are not available, sequential analysis of the percent of chimerism "may offer the only evidence on which sub-clinical relapse of disease can be assessed . . . " Kristt *et al.*, at page 261.

17. With regard to the field of parentage testing, the HITA website once again has a useful definition:

"Parentage testing is the examination and comparison of an alleged parent's and a child's genetic profiles to determine whether the individuals are biologically related as parent and child. There are two types of parentage tests: paternity tests and maternity tests."

Thus, where one is not seeking to determine the parent of a child by comparing BOTH profiles, it would not fall in the definition.

18. Certainly, monitoring bone marrow engraftment from a transplant between adults would not fall within the above-noted parentage testing definition. Moreover, even where a child and a parent are involved in the bone marrow transplant, the testing would not be "to determine whether the individuals are biologically related."

19. Thus, monitoring bone marrow engraftment using multiplex STR analysis is outside the field of parentage testing. The patient material is simply being analyzed to ensure the graft has taken hold in the recipient (and to what extent).

[redacted]

21. The AmpFISTR® Profiler Plus® PCR Amplification Kit was used to determine T cell chimerism at the Virginia Commonwealth University Medical Center (Epp *et al.*, *J. Mol. Diag.* 9(3): 665-6 (2007)) (Exhibit 5). For the reasons detailed above, it is my opinion that the use of STR multiplex kits in this manner does not fall within "Forensics and Human Identity" or "Paternity" applications.

22. The AmpFISTR® Profiler Plus® and COfiler® PCR Amplification Kits were used for monitoring chimerism using fluorescent multiplex PCR of STRs and compared the limit of detection and heterogeneity of STR loci by Genzyme Genetics, Westborough MA (Hire *et al.*, "Bone Marrow Engraftment Chimerism Monitoring by STR Analysis" 2004) (Exhibit 6). For the reasons detailed above, it is my opinion that the use of STR multiplex kits in this manner does not fall within "Forensics and Human Identity" or "Paternity" applications.

23. The AmpFISTR® Profiler® PCR amplification kit was evaluated as a clinical test to determine chimerism or reappearance of recipient blood cells during bone

marrow engraftment monitoring by John Hopkins University (Liang *et al. J. Mol. Diag*. 10: 142-6 (2008)) (Exhibit 2). For the reasons detailed above, it is my opinion that the use of STR multiplex kits in this manner does not fall within "Forensics and Human Identity" or "Paternity" applications.

24. The AmpFISTR® Profiler Plus® kit was tested with an algorithm to reduce the impact of stutter on bone marrow transplant chimerism monitoring by the University of Minnesota (Thyagarajan *et al. J Clin Lab Anal* 23:308-11 (2009)) (Exhibit 7). For the reasons detailed above, it is my opinion that the use of STR multiplex kits in this manner does not fall within "Forensics and Human Identity" or "Paternity" applications.

25. Post-transplant lymphoproliferative disorder (PTLD) is a major complication of organ transplantation. Most PTLDs following solid organ transplant are of recipient origin. PTLDs are mostly of donor origin following bone marrow or stem cell transplantation. The AmpFISTR® Identifiler® PCR amplification kit was used to determine that tumor cells from a particular patient were of donor origin by the University of Medicine & Dentistry of New Jersey (Zhang, H. *et al. Blood* (ASH Annual Meeting Abstracts) 114 Abstract 4305 (2009)) (Exhibit 8). For the reasons detailed above, it is my opinion that the use of STR multiplex kits in this manner does not fall within "Forensics and Human Identity" or "Paternity" applications.

26. The AmpFISTR® Profiler Plus® Kit was used to determine stem cell transplantation success in either the traditional ablative or the newer non-myeloablative methods of reconstitution of the patient's bone marrow with the

donor's stem cells in order to establish a complete donor chimera by the City of Hope National Medical Center (Senitzer and Giadulis, Scientific Communication: American Society For Histocompatibility and Immunogenetics (ASHI) Quarterly Second Quarter 2001) (Exhibit 9). Stem cells are the types of cells that engraft during bone marrow transplantation. For the reasons detailed above, it is my opinion that the use of STR multiplex kits in this manner does not fall within "Forensics and Human Identity" or "Paternity" applications.

27. The AmpFlSTR® Profiler® Kit was routinely used to evaluate polymorphic differences between the patient and donor that allows for quantification of chimerism after bone marrow transplantation by Johns Hopkins University (Murphy, K. M. *et al.*, *J. Mol. Diag.* 9:408-13 (2007)) (Exhibit 10). For the reasons detailed above, it is my opinion that the use of STR multiplex kits in this manner does not fall within "Forensics and Human Identity" or "Paternity" applications.

28. The ARUP clinical diagnostic laboratory headquartered in Salt Lake City, UT offers a variety of STR clinical diagnostic tests utilizing the Identifiler® Kit for bone marrow transplantation and chimerism determination. These include: Chimerism Donor (Exhibit 11); Chimerism post-transplant sorted cells (Exhibit 12); Chimerism post-transplant (Exhibit 13); and Chimerism Pre-Transplant Recipient (Exhibit 14). For the reasons detailed above, it is my opinion that the use of STR multiplex kits in this manner does not fall within "Forensics and Human Identity" or "Paternity" applications.

29. The Molecular Diagnostic Laboratory of the Barnes Jewish Hospital associated with the Washington University School of Medicine utilizes the Profiler Plus® Kit in a clinical diagnostic assay they offer for monitoring bone marrow engraftment. (Exhibit 15). For the reasons detailed above, it is my opinion that the use of STR multiplex kits in this manner does not fall within "Forensics and Human Identity" or "Paternity" applications.

30. Transplant engraftment monitoring has been expanded to types of cellular transplants not involving bone marrow or hematopoietic stem cells. A review chapter by Fisher & Mas in *Hepatocyte Transplantation* 481, Chapter 9, pages 97-105 (2009) (selected pages of which are attached as Exhibit 16) provides directions for the use of the Profiler Plus® Kit for monitoring of liver engraftment of hepatocyte infusions for correction liver deficiencies. For the reasons detailed above, it is my opinion that the use of STR multiplex kits in this manner does not fall within "Forensics and Human Identity" or "Paternity" applications.

b. genotyping hydatidiform moles and managing GTD

31. Multiplex STR analysis can be very useful in other clinical situations, such as genotyping hydatidiform moles. See K. Murphy *et al.*, "Molecular Genotyping of Hydatidiform Moles," *J. Mol. Diag.* 11:598-605 (2009) (attached hereto as Exhibit 17). Unfortunately, distinguishing between different types of moles based on morphology is difficult, with groups reporting "poor interobserver and intraobserver reproducibility." See F. Lipata *et al.*, "Precise DNA Genotyping Diagnosis of Hydatidiform Mole," *Obstetrics & Gynecol.* 115(4): 784-94 (2010)

(introduction section) (attached hereto as Exhibit 18). The commercially available Applied Biosystems (AB) multiplex STR analysis kits have been found to be "applicable to routine practice for classifying molar specimens" See K. Murphy *et al.*, Molecular Genotyping of Hydatidiform Moles, *J. Mol. Diag.* 11:598-605 (2009) at p. 604 (attached hereto as Exhibit 17).

32. Distinction of hydatidiform moles from non-molar specimens and the sub-classification of hydatidiform moles as complete ("CHM") or partial ("PHM"), are important for both clinical practice and investigational studies. Accurate classification is critical to ascertaining the woman's risk of persistent gestational trophoblastic disease (GTD) and determining the appropriate nature and duration of clinical follow-up care. Both under-diagnosis and over-diagnosis of hydatidiform moles can result in faulty estimation of the risk of persistent GTD and improper clinical management.

33. The fundamental question involved in classifying molar specimens using multiplex STR analysis is not: who is this person? It is not for the purpose of human identity because, after all, the identity of the person with the potential molar pregnancy is known. It is also not for the purpose of determining the father. Rather, it is done to determine whether mother is at risk for more serious disease.

34. The AmpFlSTR® Profiler® Kit was used for the molecular genotyping of hydatidiform moles from stored historical samples to determine their classification by Johns Hopkins University (Murphy et al., *J. Mol. Diag.* 11:598-605 (2009)) (Exhibit 17). For the reasons detailed above, it is my opinion that the

use of STR multiplex kits in this manner does not fall within "Forensics and Human Identity" or "Paternity" applications.

35. The AmpFlSTR® Identifiler® PCR Amplification Kit was used to diagnose and subtype hydatidiform moles by Yale University (Lipata et al., *Obstetrics & Gynecol* 115(4): 784-94 (2010)) (Exhibit 18). For the reasons detailed above, it is my opinion that the use of multiplex STR amplification kits in this manner does not fall within "Forensics and Human Identity" or "Paternity" applications.

36. The AmpFlSTR® Identifiler® PCR Amplification Kit was used to demonstrate the applicability of DNA genotyping as a molecular approach for the diagnosis, and subtyping of molar pregnancy in daily clinical practice by Yale University (Bifulco et al., *Am J Surg Pathol* 32:445–451 (2008)) (Exhibit 19). For the reasons detailed above, it is my opinion that the use of multiplex STR amplification kits in this manner does not fall within "Forensics and Human Identity" or "Paternity" applications.

37. Choriocarcinoma is a malignant, trophoblastic and aggressive form of cancer. It often arises in patients with a previous history of hydatidiform moles. The AmpFlSTR® Profiler Plus® kit was evaluated for diagnosis of gestational and non-gestational choriocarcinomas and differentiation from both benign and malignant tissues of other types including partial and complete hydatidiform moles. Samples had been preserved in paraffin blocks and were separated by microdissection at the Henry Ford Hospital (Cankovic *et al. Gynecol Oncol* 103:614-7 (2006)) (Exhibit 20). For the reasons detailed above, it is my opinion

that the use of the Profiler Plus® STR kits in this manner does not fall within "Forensics and Human Identity" or "Paternity" applications.

38. Gestational Trophoblastic Neoplasm (GTN) is a group of neoplastic diseases composed of choriocarcinomas, placental site trophoblastic tumors, and epithelioid trophoblastic tumors, all of which are derived from fetal trophoblastic tissue. The AmpFlSTR® Profiler® kit was used for sex determination of GTN samples by Johns Hopkins University (Yap et al., *J. Oncology* Volume 2010, Article ID 364508) (Exhibit 21). The majority of samples lacked Y chromosomes suggesting that they arose from earlier complete hydatidiform molar pregnancies. For the reasons detailed above, it is my opinion that the use of multiplex STR amplification kits in this manner does not fall within "Forensics and Human Identity" or "Paternity" applications.

39. The AmpFISTR® Profiler Plus® and COfiler® PCR amplification kits were used to determine the zygosity of a hydatidiform mole and to rule out maternal cell contamination thereby elucidating the diagnosis of a complete hydatidiform mole and a co-existing normal fetus by Genzyme Genetics, Westborough, MA (Faulkner *et al.* "Utility of Molecular Zygosity Analysis to Determine the Genetic Composition of a Twin Pregnancy with an Apparent Hydatidiform Mole") (Exhibit 22). For the reasons detailed above, it is my opinion that the use of STR multiplex kits in this manner does not fall within "Forensics and Human Identity" or "Paternity" applications.

40. The AmpFlSTR® Profiler® Kit was used to diagnose hydatidiform moles to distinguish partial (PHM) and complete (CHM) types from one another as well as

from non-molar abortuses (NMA) by Johns Hopkins University (Hafez *et al.*, J. Mol. Diag. 9: 691 (2007) (Abstract)) (Exhibit 23). For the reasons detailed above, it is my opinion that the use of STR multiplex kits in this manner does not fall within "Forensics and Human Identity" or "Paternity" applications.

41. The AmpFlSTR® Profiler® and AmpFlSTR® Identifiler® kits were used to perform molecular genotyping, which determined that a sample from a spontaneous abortion exhibited biparental diploidy with trisomies of chromosomes 7, 13, and 20, all of paternal origin. The sample demonstrated abnormal villous morphology indicating that this sample with excess paternal genetic material had some characteristics of a partial hydatidiform mole. This diagnosis was reported by Johns Hopkins University (Kirby-Norris *et al.*, *J Mol Diag* 1: 620 (2009) (Abstract)) (Exhibit 24) and (Kirby-Norris *et al.*, *J Mol Diag* 12:525-9 (2010) (Abstract)) (Exhibit 25). For the reasons detailed above, it is my opinion that the use of multiplex STR amplification kits in this manner does not fall within "Forensics and Human Identity" or "Paternity" applications.

42. The ARUP clinical diagnostic laboratory headquartered in Salt Lake City, UT offers a clinical diagnostic test utilizing the Identifiler® Kit to detect molar pregnancies called: Molar Pregnancy, 16 DNA Markers, 0051755. (Exhibit 26). For the reasons detailed above, it is my opinion that the use of multiplex STR amplification kits in this manner does not fall within "Forensics and Human Identity" or "Paternity" applications.

c. cancer analysis

43. The analysis of STRs is very useful for understanding a variety of cancers in addition to choriocarcinoma. The AmpFlSTR® Identifiler® kit was used to analyze genetic instability in a variety of different cancers by detecting allelic imbalance. In a set of 239 tumor samples, 67% contained two or more STR loci demonstrating allelic instability. This work was performed at the University of New Mexico (Heaphy *et al.*, *J. Mol. Diag.* 9(2):266-271 (2007)) (Exhibit 27). For the reasons detailed above, it is my opinion that the use of multiplex STR amplification kits in this manner does not fall within "Forensics and Human Identity" or "Paternity" applications.

44. The AmpFlSTR® Identifiler® PCR Amplification Kit was used to demonstrate that Exaggerated Placental Site reaction, a non-neoplastic condition, is not a precursor to Placental Site Trophoblastic Tumor (PSTT), a true neoplastic proliferation of intermediate trophoblasts in clinical research performed by the Harvard and Yale University Medical Schools (Jorge and Hui, *Int. J. Gynecol. Path.* 27:562-7 (2008)) (Exhibit 28). For the reasons detailed above, it is my opinion that the use of multiplex STR amplification kits in this manner does not fall within "Forensics and Human Identity" or "Paternity" applications.

45. A clinical research study published by Carvalho *et al.*, in *DNA and Cell Biol.* 29(1):3-7 (2010) (Exhibit 29) discovered that some of the Y-chromosome STR alleles analyzed by the Yfiler® Kit were associated with the occurrence of prostate cancer. They propose that the Yfiler® Kit can be used as a clinical

diagnostic assay for prostate cancer risk. For the reasons detailed above, it is my opinion that the use of multiplex STR amplification kits in this manner does not fall within "Forensics and Human Identity" or "Paternity" applications.

d. cell culture authentication

46. Multiplex STR analysis is also useful to assist in confirming that cell lines thought to be independently derived are in fact genetically unique. This is useful in a variety of settings, including clinical research and basic research. In one study, multiplex STR analysis with commercially available AB kits was performed on 40 reported thyroid cancer-derived cell lines, only to reveal that a) many were not unique, and b) some were not even of thyroid origin. See R. Schweppe *et al.*, "Deoxyribonucleic Acid Profiling Analysis of 40 Human Thyroid Cancer Cell Lines Reveals Cross-Contamination Resulting in Cell Line Redundancy and Misidentification," *J. Clin. Endocrinol. Metab.* 93:4331-41 (2008) (attached hereto as Exhibit 30) (see Abstract). As noted in this report (p. 4332), the NIH now recognizes this problem and requires a commitment to use of cell authentication with all grant applications.

47. Cell line authentication by multiplex STR analysis is a type of tissue typing. In general, tissue typing is the analysis of various markers capable of characterizing the similarities and differences between tissues from different individuals. Historically, the term has been frequently used in conjunction with organ transplantation where various immunological markers are typed to match tissues to avoid transplant rejection. More recently, STR typing and other methods of

DNA typing have become methods of tissue typing of increasing utilization in research and clinical diagnostics as reflected in the discussion above. Use of multiplex STR analysis for cell line authentication is not human identity testing because the purpose for testing the cell line is not for identification of the person from whom the cell line was established. Rather, its purpose is to confirm that the intended cell line is actually the one involved in the research and is a measure of the genetic integrity of the cell line. In cases where new cell lines are being established or studied, multiplex STR analysis is used to establish that the new cell lines are unique.

48. Cell line authentication is not a problem related to forensic or paternity testing. It is not a problem for human identity testing since the fundamental question is not: who is this person? It has become an essential research application because use of an incorrect cell line can invalidate a researcher's published data.

49. The AmpFlSTR® Profiler® Plus Kit was used to genetically profile 40 presumptive thyroid cancer cell lines wherein only 23 were found to be unique by the University of Colorado (Schweppe *et al.*, *J Clin Endocrinol Metab*, 93(11):4331– 41 (2008)) (Exhibit 30). For the reasons detailed above, it is my opinion that the use of multiplex STR amplification kits in this manner does not fall within "Forensics and Human Identity" or "Paternity" applications.

50. The AmpFlSTR® Identifier® PCR Amplification Kit was used to verify cell line identities by the University of Arizona (Shaw *et al.*, *J Pharmacol Exp Therapeut* 331(2):636-647 (2009)) (Exhibit 31). For the reasons detailed above, it is my

opinion that the use of multiplex STR amplification kits in this manner does not fall within "Forensics and Human Identity" or "Paternity" applications.

51. The AmpFlSTR® Identifiler® PCR Amplification Kit was used to test and authenticate thyroid cell lines used to explore the mechanism of gene expression changes in thyroid tumor samples by the University of Pittsburgh (Zuo *et al.*, Cancer Research 70(4); 1389–97 (2010)) (Exhibit 32). For the reasons detailed above, it is my opinion that the use of multiplex STR amplification kits in this manner does not fall within "Forensics and Human Identity" or "Paternity" applications.

52. The AmpFlSTR® Identifiler® Kit was used to validate the MDA- MB231 breast cancer cell line by the M.D. Anderson Cancer Center (Iadevaia et al., Cancer Resesarch 70(17):OF1–11 (2010)) (Exhibit 33). For the reasons detailed above, it is my opinion that the use of multiplex STR amplification kits in this manner does not fall within "Forensics and Human Identity" or "Paternity" applications.

53. The AMPFlSTR® Identifiler® Kit was used to distinguish human embryonic stem cell lines, even after genetic modification and in different culture conditions by Rutgers University (Cardoso et al., Poster) (Exhibit 34). For the reasons detailed above, it is my opinion that the use of multiplex STR amplification kits in this manner does not fall within "Forensics and Human Identity" or "Paternity" applications.

54. The AMPFlSTR® Identifiler® Kit was and is used to provide human cell line authentication services by Biosynthesis, Inc. (http://www.biosyn.com/ celllinetesting.aspx) (an excerpt from this website is attached as Exhibit 35). For

the reasons detailed above, it is my opinion that the use of multiplex STR amplification kits in this manner does not fall within "Forensics and Human Identity" or "Paternity" applications.

55. The AMPFlSTR® Identifiler® Kit was and is used to provide DNA profiling services, including cell line authentication, by the University of Colorado (http://loki.ucdenver.edu/DNA_Profiling.htm) (an excerpt from this website is attached as Exhibit 36). For the reasons detailed above, it is my opinion that the use of multiplex STR amplification kits in this manner does not fall within "Forensics and Human Identity" or "Paternity" applications.

56. The AmpFlSTR® Identifiler® PCR Amplification Kit was and is used to provide cell line authentication services by Johns Hopkins University (http://faf.grcf.jhmi.edu/str.html) (an excerpt from this website is attached as Exhibit 37). For the reasons detailed above, it is my opinion that the use of multiplex STR amplification kits in this manner does not fall within "Forensics and Human Identity" or "Paternity" applications.

57. The AmpFlSTR® Identifiler® PCR Amplification Kit was and is used to provide cell line authentication services by The University of Arizona (http://uagc.arl.arizona.edu/index.php/dnacell-fingerprinting.html) (an excerpt from this website is attached as Exhibit 38). For the reasons detailed above, it is my opinion that the use of multiplex STR amplification kits in this manner does not fall within "Forensics and Human Identity" or "Paternity" applications.

58. The AmpFlSTR® Identifiler® PCR Amplification Kit was and is used to provide cell line authentication services by The University Of Pittsburg (University of

Pittsburgh Cancer Institute Cell Culture and Cytogenetics Facility website: http://www.upci.upmc.edu/cytogen/serv.cfm) (an excerpt from this website is attached as Exhibit 39). For the reasons detailed above, it is my opinion that the use of multiplex STR amplification kits in this manner does not fall within "Forensics and Human Identity" or "Paternity" applications.

59. The AmpFlSTR® Identifiler® PCR Amplification Kit (Applied Biosystems) was and is used to perform cell line authentication by determining the unique genetic signature of each of several new cell lines by Rutgers University (Moore *et al.*, Stem Cell Research 4:92–106 (2010)) (Exhibit 40). For the reasons detailed above, it is my opinion that the use of multiplex STR amplification kits in this manner does not fall within "Forensics and Human Identity" or "Paternity" applications.

60. The AmpFlSTR® Identifiler® PCR Amplification Kit (Applied Biosystems) was and is used to provide cell line authentication services by SeqWright DNA Technology Services (http://www.seqwright.com/researchservices/humancellline.html) (an excerpt from this website is attached as Exhibit 41). For the reasons detailed above, it is my opinion that the use of multiplex STR amplification kits in this manner does not fall within "Forensics and Human Identity" or "Paternity" applications.

61. The AmpFlSTR® Identifiler® Kit was and is used to perform cell line authentication for genetic identification of cell lines and xenografts by the Children's Oncology Group Cell Culture and Xenograft Repository (http://www.cogcell.org/clid.shtml) (an excerpt from this website is attached as

Exhibit 42). For the reasons detailed above, it is my opinion that the use of multiplex STR amplification kits in this manner does not fall within "Forensics and Human Identity" or "Paternity" applications.

62. The AmpFlSTR® Identifiler® Kit was and is used to perform cell line authentications by the University of Southern California (Cabral *et al.*, Proc Am Assoc Cancer Res 48:96 (2007)) (Exhibit 43). For the reasons detailed above, it is my opinion that the use of multiplex STR amplification kits in this manner does not fall within "Forensics and Human Identity" or "Paternity" applications.

63. A similar application involves the use of STR analysis to confirm the identification of biopsy specimens in clinical research and clinical diagnostics. In clinical research reported by Dong *et al.*, from the Emory University School of Medicine in *Human Mol. Genet.* 17(7):1031-42 (2008) (Exhibit 44), the Identifiler® Kit was used to confirm that paired samples of prostate cancer tissue and normal tissue believed to have been taken from the same patient were in fact from the same patient. These confirmation tests are used to rule out contamination or misidentification of surgical biopsy samples in the clinical diagnostic laboratory are sometimes referred to as specimen provenance testing. The purpose of the test is not to identify an individual but to confirm the identity and source of the biopsy sample. For the reasons detailed above, it is my opinion that the use of multiplex STR amplification kits in this manner does not fall within "Forensics and Human Identity" or "Paternity" applications.

e. determination of fetal sex

64. For a number of diseases where the causative gene is on the X-chromosome (X-linked diseases) determination of the sex of the fetus at very early stages of development is of great importance. Female fetuses have two X chromosomes and are less likely to be affected by recessive X-linked disease genes. The parental relationship of the fetus is not important in these cases - only its sex. AmpFlSTR® Identifiler® and Yfiler® Kits were used to develop a new diagnostic test for fetal sex utilizing fetal DNA present in maternal plasma. (Wagner *et al.*, *Prenatal Diagnosis* 28:412-6 (2008))(Exhibit 45). The Yfiler® Kit was found to provide a more reliable assay. For the reasons detailed above, it is my opinion that the use of multiplex STR amplification kits for clinical research or clinical diagnosis in this manner does not fall within "Forensics and Human Identity" or "Paternity" applications.

f. archeological and anthropological research

65. The Y-chromosome is particularly useful in studies of ancient peoples and their geographical migration at different periods of time in history. Most of the Y-chromosome contains DNA sequences that have no similar sequences (homologs) on other chromosomes. Also, only a single copy of the Y-chromosome at most exists in any cell. Therefore, recombination is greatly suppressed and large segments of the Y-chromosome DNA sequence are passed from generation to generation unchanged. Analysis of STR alleles at different Y-chromosome loci

demonstrate patterns of co-inheritance that allow these relatively unchanging segments of DNA to be identified. These patterns of inheritance are referred to as haplotypes. The slow rate of change of Y-haplotypes allows the study of the geographical movement of men carrying these Y-chromosomes over long periods of history.

66. The Yfiler® Kit was used to study the relationship between different Tamil castes in India compared to other populations around the world. (Balamurugan *et al.*, Legal Medicine 12:265-9 (2010)(Exhibit 46). There was no determination of paternity in this study and no attempt to identify any person as all individuals involved were volunteers known to the researchers. For the reasons detailed above, it is my opinion that the use of multiplex STR amplification kits in this manner does not fall within "Forensics and Human Identity" or "Paternity" applications.

67. The Yfiler® Kit was used to determine the number of Y-haplotypes present in the Mendoza population of Argentina in a research study published by Marin & Furfuo in *Forensic Sci. Int'l.: Genetics* 4:e89-93 (2010)(Exhibit 47). They studied the impact of historical European migration on the male population of this group of people. A similar study using the Yfiler® Kit concerning the population of South-East Romania was reported by Stanciu *et al.* in *Legal Medicine* 12:259-64 (2010) (Exhibit 48). A similar study using the Yfiler® Kit concerning the population of Yakutia was reported by Theves *et al.* in *Forensic Sci. Int. Genet.* (2010) (Exhibit 49). A similar study using the Yfiler® Kit concerning the population of the El Beni Department of North Bolivia was reported by Tirado *et*

al. in *Legal Medicine* 11:101-3 (2009) (Exhibit 50). A similar study using the Yfiler® Kit concerning the population of South Poland was reported by Wolanska-Nowak *et al.* in *Forensic Sci. Int. Genet.* 4:e43-4 (2009) (Exhibit 51). Vermeulen *et al.* in *Forensic Sci Int. Genet* 3:205-13 (2009) (Exhibit 52) studied the historical relatedness of men from populations around the world using the Yfiler® Kit. Paternity relationships were not studied and no individuals were identified as a result of the studies. For the reasons detailed above, it is my opinion that the use of multiplex STR amplification kits in this manner does not fall within "Forensics and Human Identity" or "Paternity" applications.

g. clinical research on inherited genetic and acquired diseases

68. Twins are often utilized in studies of the inheritance of genetic risk factors for various human genetic diseases. Zygosity or the relationship between the twins is studied to confirm that they are in fact twins and to differentiate identical from fraternal twins. A study of genetic and environmental influences on increased plasma homocysteine utilized the Profiler Plus® Kit to determine zygosity. (Bathum *et al*, Clin. Chem. 53(5):971-9 (2007)) (Exhibit 53). The kit was not used to determine parentage or to identify any individual. For the reasons detailed above, it is my opinion that the use of multiplex STR amplification kits in this manner does not fall within "Forensics and Human Identity" or "Paternity" applications.

69. The Profiler Plus® Kit was instrumental in a clinical research study that indicated a role for chimerism in the early stages of development of thyroid autoimmunity

in twins. The kit was used to confirm and analyze the nature of the zygosity of a large number of twins that participated in this study. (Brix *et al.*, J Clin Endocrinol. Metab. 94(11)4439-43 (2009)) (Exhibit 54). There was no determination of parentage or identification of individuals in this study. For the reasons detailed above, it is my opinion that the use of multiplex STR amplification kits in this manner does not fall within "Forensics and Human Identity" or "Paternity" applications.

70. The Profiler® Kit was used to analyze twin zygosity in a clinical research study entitled, "Interactions Between Secondhand Smoke and Genes That Affect Cystic Fibrosis Lung Disease," by Collaco *et al.*, in *JAMA* 299(4):417-24 (2008) (Exhibit 55). For the reasons detailed above, it is my opinion that the use of multiplex STR amplification kits in this manner does not fall within "Forensics and Human Identity" or "Paternity" applications.

B. Tutorial Regarding the STR Technology At Issue

71. In this section, I have attempted to assist the Court in understanding the STR technology by providing a brief tutorial.

72. The human genome is comprised of the DNA present in the 23 pairs of chromosomes existing in the nucleus of human cells. This genomic DNA is made of two complementary "strands" or "sequences" of "nucleotides" or "bases." The nucleotides in DNA are only four in number and are paired in a defined manner. The four nucleotides are adenine (A), thymine (T), guanine (G) and cytosine (C). An (A) is complementary to, and pairs only with (T); a (C) is complementary to, and pairs only with a (G).

73. The combinations of genetic information present at multiple locations in genomic DNA are unique to each individual. It is this fact that forms the premise for genetic identity testing. To use DNA to identify an individual, or cell line, or tissue sample, one can target and identify certain locations or "loci" on the chromosomes which are polymorphic within a population, i.e., loci that vary from individual to individual within the population. These loci are useful as identifiers only when they exhibit a high degree of variation within the population, since if they were largely the same from individual to individual within the population, their ability to distinguish any one individual from another would be minimal.

74. The more a specified locus varies within a population, i.e., the more it varies from individual to individual, the more "polymorphic" the locus is said to be. No one locus alone, however, will positively identify an individual to a statistically significant degree, since no one locus is unique to each individual within any given population. Consequently, for purposes of forensic and paternity determinations, the identification of multiple polymorphic loci is necessary. Indeed, the more polymorphic the loci used in the identification process, the more accurate the identification becomes because the statistical probability of a match between the DNA sample and the individual in question increases exponentially as additional matching loci are identified.

75. The goal is to use enough loci with sufficient polymorphic characteristics such that the identification is so statistically significant that the result cannot be reasonably disputed, i.e., the individual is identified beyond any reasonable doubt. For example, using Promega's genetic identity products, one can identify an

individual's DNA with a power of discrimination exceeding 1 in 100,000,000,000. However, where the DNA sample is of poor quality, the power of discrimination can be less than this.

76. STRs are loci found within genomic DNA that have a number of short repetitive nucleotide sequences. Different authors have slightly different definitions with regard to the repeat length that is considered an STR. Any differences in these definitions, however, do not appear to have impact on any issues in this case.

77. The DNA sequences at a particular STR locus (singular form of loci) within a given population will exhibit a variable number of these repeat sequences. For some individuals within a given population the sequence will repeat 7 times, for others 8 times, for others 4 and so on. It is this variation in the number of repeats at a particular locus that is responsible for the polymorphism, which permits scientists to genetically distinguish one individual from another.

78. The particular genetic information or base sequence associated with a segment of DNA at a particular STR locus in one individual is called an "allele." The alleles are numbered in accordance with the number of repeated nucleotide motifs (the "motif" is the specific repeated nucleotide sequence, e.g., AATG, of the short tandem repeat).

79. To understand the meaning of the term "co-amplifying" in step (c) of the various independent method Claims of the Promega Patents, it is helpful to understand the commonly known term "amplifying." The term "amplify" refers to a process in which multiple copies of the alleles present at the STR loci are made. The STR regions of the DNA must be "amplified" to be visualized or detected because they

are present in too low a concentration to be detected among the rest of the human DNA.

80. PCR is one method of amplifying. There are several steps in the PCR process. First, the "double stranded" or two strands of genomic DNA are separated or "denatured," thereby forming "single stranded" DNA. This denaturation step is done by heating the DNA to a certain temperature, which is sufficient to cause the two strands to separate. Second, a pair of PCR "primers" is introduced and allowed to hybridize or pair with the single stranded DNA. "Hybridization" occurs when the PCR primers "anneal" or join to a single strand of the DNA. This hybridization occurs in accordance with the nucleotide pairing rules (e.g. A with T, etc.) noted above, i.e., at a point on the single stranded DNA where the PCR primer sequence is complementary to the genomic nucleotide sequence. Referring to the two opposing primers as the "forward" or "reverse" PCR primer differentiates each primer in the pair.

81. There is a definition of "primers" or "primer" in the specifications of all of the Promega Patents and these definitions are consistent with how the term is understood to one skilled in the art.

82. The PCR primers hybridize at points on the genomic DNA that are adjacent to, or "flank," the actual STR locus. These "flanking regions" are used as the point of hybridization because they are not polymorphic, i.e., they contain the same sequence of nucleotides for all individuals within a given population even though the number of repeats contained in the STR locus between the flanking regions

varies from individual to individual. This ensures that all alleles in all individuals will be amplified.

83. The third step of the PCR process is extension of the primers that have hybridized to the single stranded DNA molecules to convert them into double stranded molecules. An enzyme known as a "DNA polymerase" accomplishes this extension process. The polymerase reads the sequence of the single stranded DNA beginning at the primer location and attaches the complementary nucleotides to the primer guided by the opposite strand (As to Ts and Cs to Gs), thereby making it double stranded. At this point the number of copies of each allele has doubled. These three steps are then repeated many times to amplify the locus of interest.

84. Amplifying the alleles present at a single STR locus is commonly referred to as a "monoplex" reaction. If one wanted to use eight STR loci in an analysis of a particular sample, one could carry out eight separate monoplex reactions amplifying eight separate STR loci. Use of monoplex PCR was the initial method employed when analyzing STR loci for DNA analysis. However, analysis of many STR loci using monoplex PCR is not practical, since it requires more DNA than is present in many forensic samples.

85. Multiplex PCR is key to realizing the advantages of STRs for determining genetic identity. Often, one must be able to analyze multiple STRs from a relatively small amount of sample. That could only be accomplished if it were possible to multiplex the amplification of STR alleles in such a way that you could still

determine all of the alleles present at each locus. The technology of the Promega Patents accomplished that result.

86. To determine the amplified alleles that are present following amplification, they are typically segregated from the amplification (e.g. PCR) reaction mixture or otherwise individually detected. One such process used to separate the alleles is known as "electrophoresis." Polyacrylamide gel electrophoresis (PAGE) is one type of electrophoresis that can be used. Capillary gel electrophoresis (CE) is another type of electrophoresis that can be used.

87. While the term "gel" is used in the various patents of this case, the nature of the gel need not be (and often is not) the same for each technique. Agarose gels used to separate DNA are not crosslinked and typically comprise between 1 and 3% agarose, which is a linear polymer made up of disaccharide (sugar) units. Polyacrylamide gels used in slab gels (discussed more below) are typically crosslinked.

88. Uncrosslinked polyacrylamide (or a derivative thereof) is frequently used in CE. While one might be tempted not to call this material a "gel" because it may not be semi-solid, a number of people in the field refer to this material as a gel. For example, the authors of Chapter 16 of Landers *et al.* refer to such materials as gels: "The development of replaceable non-crosslinked or linear polyacrylamide gels for DNA sequencing was probably the most significant advance made in the field of CE during the 1990s. In replaceable gels, a dynamic network of entangled linear polymers forms the pores through which the DNA is sieved." See Chapter 16: "DNA Sequencing by Capilllary Electrophoresis," by David Yang *et*

al., In: *Handbook of Capillary and Microchip Electrophoresis and Associated Microtechniques*, Third Edition, James P. Landers (Editor), CRC Press, 2007 (ISBN-10: 0849333296) (Exhibit 56) (underlining added). Similarly, the standard Forensic text by Butler refers to such material as gels: "Prior to injecting each sample, a new gel is 'poured' by filling in the capillary with a fresh aliquot of the polymer solution. The CE can be thought of as a long, skinny gel that is only wide enough for one sample at a time." Forensic DNA Typing Biology, Technology, and Genetics of STR Markers, Second Edition by John Butler, Elsevier, Academic Press, 2005 (p.319) (Exhibit 57) (underlining added).

89. The polyacrylamide gel electrophoresis (or "PAGE") process typically involves the preparation of a polyacrylamide gel between two glass plates, where the gel polymerizes to form a so-called "slab gel." The amplified alleles are then applied to a "well" at the top of the gel, and an electric current is applied to the gel. The amplified alleles will move down the lane below the well, with smaller DNA amplification products (i.e., lower molecular weight products) that contain the amplified STR alleles moving down the gel faster than the larger amplification products (i.e. higher molecular weight products). The various different sizes of the amplification products are separated in this fashion and appear as "bands" on the gel. In CE each capillary acts like a lane in a slab gel and the process of separation relies on the same principles.

90. The alleles from one DNA sample can then be compared to the alleles of a second DNA sample by, for example, running the two samples side-by-side on the gel. One can then determine whether or not the alleles in two samples are consistent

with the samples originating from the same individual. Additionally a "size marker" or "allelic ladder" is often run concurrently with the sample either mixed with the sample (size marker) or in another lane of the gel (allelic ladder). The size standard allows precise determination of allele size and reduces variability between lanes or CE capillaries. By comparing the size of alleles amplified from the DNA sample to the size of the alleles in the allelic ladder one can determine precisely which alleles are present in the DNA sample.

91. Like the PAGE technique, separation of the PCR products using capillary gel electrophoresis or CE is based primarily on size. There is nothing in the specifications of the Promega Patents to suggest that the "capillary gel" must be cross-linked. POP-4, which is employed in the examples of the '235 Patent comprises so-called "entangled poly(N,N-dimethylacrylamide)" (or PDMA) which is not cross-linked.

92. The '984 Tautz Patent primarily uses the term "gel" in its unmodified general sense throughout the specification and in the claims. For example Claim 25 is limited only to "a suitable electrophoretic gel," which would be understood by one skilled in the art to include both non-cross-linked (e.g. agarose, entangled PDMA, etc.) and cross-linked gels.

93. The '984 Tautz Patent refers to "direct repeats" and "irregularly direct repeats" (i.e. cryptically simple repeats). A direct repeat is one that is in the same orientation as the index sequence. For example, CAG…..CAG is a direct repeat; CAG…GAC is an inverted repeat. What makes a direct repeat a simple sequence is that it is a tandem repeat. A tandem repeat is a repeat with no intervening

nucleotides. For example, CAGCAG is a direct tandem CAG repeat, while CAGTCAG is a non-tandem or irregular direct repeat (i.e. cryptically simple repeat).

94. The underlined portion with arrows underneath in Fig 2 of the Tautz Patent is a simple repeat of 8 base pairs GCTAACTA. There are two tandem copies so it is a simple repeat.

95. CODIS is a database system that stores information about the alleles present in individuals that have been STR typed by the FBI or State crime laboratories. The database stores information on particular STR loci including those that make up the CODIS standard 13 loci. For specific CODIS STR loci (Exhibit 58) one can look on the web to determine the repeat structure (see Exhibit 59a through 59n). For example, http://www.cstl.nist.gov/strbase/str_D5S818.htm show the repeat structure for D5S818, which is a CODIS STR locus (Exhibit 59d). When one looks at the column listing the "Repeat Structure" one sees that all of the alleles with sequences shown are simple repeats. By contrast, when one looks at http://www.cstl.nist.gov/strbase/str_D21S11.htm, which is CODIS STR, D21S11, one finds all of the alleles at this locus are cryptically simple repeats of various types (Exhibit 59m).

C. ABI/LifeTech Kits and Protocols

ABI/LT Identifiler® Kit

96. The Product Insert for the ABI Identifiler® PCR Amplification Kit (Exhibit 60) lists "PCR Reaction Mix" (which contains the triphosphates in a PCR buffer),

primer sets, AmpliTaq Gold® DNA Polymerase, and "Control DNA 9947A" among the components of the kit. Clearly these are reagents for performing a PCR amplification reaction. While the control DNA is provided, the test DNA is not in the kit and is provided by the particular lab where the kit will be used. The primers will anneal to this test DNA as part of the PCR reaction. The kits are indicated as able to "amplify and type" in the context of an ABI PRISM machine. *AmpFlSTR® Identifiler® PCR Amplification Kit, Product P/N 4322288 Insert P/N 4322638 REV G.*

97. The Product Insert for AB Identifiler® Kit (Exhibit 60) indicates that a certain amount of "input sample DNA" is needed for good results: "The recommended range of input sample DNA is approximately 0.5-1.25 ng. At Applied Biosystems, the kit components have been used successfully to type samples containing less than 0.5 ng of human DNA." *AmpFlSTR® Identifiler® PCR Amplification Kit, Product P/N 4322288 Insert P/N 4322638 REV G* [underlining added].

98. The User's Manual for the AB Identifiler® Kit (Exhibit 61) illustrates the point that samples that possess low amounts of template DNA (i.e. < 0.1ng) are subject to allele drop-out. *AmpFlSTR® Identifiler® PCR Amplification Kit User's Manual, Copyright 2006, 2010 Applied Biosystems* [Figure 4-12].

99. The User Manual for the AB Identifiler® Kit (Exhibit 61) indicates the kit permits one to multiplex (i.e. co-amplify) multiple loci in a single amplification using the "polymerase chain reaction" (PCR): "By adding an additional dye, more loci can be multiplexed in a single PCR amplification as compared to the previous 4-dye

system." *AmpFlSTR® Identifiler® PCR Amplification Kit User's Manual, Copyright 2006, 2010 Applied Biosystems* pg 1-2 [underlining added].

100. The User Manual for the AB Identifiler® Kit (Exhibit 61) discusses the degree of amplification of each locus within a "co-amplified" system. *AmpFlSTR® Identifiler® PCR Amplification Kit User's Manual, Copyright 2006, 2010 Applied Biosystems* pg 4-34.

101. The User Manual for the AB Identifiler® Kit (Exhibit 61) makes the distinction between amplifying each locus alone and the situation where the loci are "co-amplified with the *AmpFlSTR* Identifiler kit." *AmpFlSTR® Identifiler® PCR Amplification Kit User's Manual, Copyright 2006, 2010 Applied Biosystems* pg 4-36 and pg 4-37.

102. The Product Insert for the Identifier® Kit (Exhibit 60) indicates that the kit provides primers that are covalently labeled: "1 tube containing locus specific 6FAM™, VIC®, NED™, and PET® dye-labeled and unlabeled primers in buffer that amplify the STR loci CSF1PO, D2S1338, D3S1358, D5S818, D7S820, D8S1179, D13S317, D16S539, D18S51, D19S433, D21S11, FGA, TH01, TPOX, vWA, and the gender marker, Amelogenin." *AmpFlSTR® Identifiler® PCR Amplification Kit Product P/N 4322288 Insert P/N 4322638 REV G* [underlining added]. All of these STR loci contain tetranucleotide or 4 base pair repeat regions.

103. The User's Manual for the Identifiler® Kit (Exhibit 61) indicates that the dyes are fluorescent labels: "The fluorescent dyes attached to the primers are light-sensitive. Protect the AmpFlSTR Identifiler Primer Set from light when not in use. Amplified DNA, AmpFlSTR® Identifiler™ Allelic Ladder and GeneScan™-

500 LIZ™ Size Standard should also be protected from light." *AmpFlSTR® Identifiler® PCR Amplification Kit User's Manual, Copyright 2006, 2010 Applied Biosystems* pg 1-7 [underlining added].

104. The User's Manual for the Identifiler® Kit (Exhibit 61) indicates that the kit provides a means to detect separated alleles using fluorescence detection: "The Identifiler kit uses a five-dye fluorescent system for automated DNA fragment analysis." The PCR products are "electrophoretically separated" and "detected" on the ABI PRISM instrument. *AmpFlSTR® Identifiler® PCR Amplification Kit User's Manual, Copyright 2006, 2010 Applied Biosystems, pg 1-2 and 3-1. (underlining added).*

105. The Product Insert for the Identifier® Kit (Exhibit 60) is identified as providing an allelic ladder comprising amplified alleles that are covalently labeled: "1 tube of AmpFlSTR® Identifiler® Allelic Ladder containing the following amplified alleles. 6-FAM™ dye (blue): D8S1179 alleles 8-19; D21S11 alleles 24, 24.2, 25-28, 28.2, 29, 29.2, 30, 30.2, 31, 31.2, 32, 32.2, 33, 33.2, 34, 34.2, 35, 35.2, 36-38; D7S820 alleles 6-15; CSF1PO alleles 6-15. VIC® dye (green): D3S1358 alleles 12-19; TH01 alleles 4-9, 9.3, 10, 11, 13.3; D13S317 alleles 8-15; D16S539 alleles 5, 8-15; D2S1338 alleles 15-28. NED™ dye (yellow): D19S433 alleles 9-12, 12.2, 13, 13.2, 14, 14.2, 15, 15.2, 16, 16.2, 17, 17.2; vWA alleles 11-24; TPOX alleles 6-13; D18S51 alleles 7, 9, 10, 10.2, 11-13, 13.2, 14, 14.2, 15-27. PET® dye (red): Amelogenin alleles X and Y; D5S818 alleles 7-16; FGA alleles 17-26, 26.2, 27-30, 30.2, 31.2, 32.2, 33.2, 42.2, 43.2, 44.2, 45.2, 46.2, 47.2, 48.2, 50.2, 51.2."

AmpFlSTR® Identifiler® PCR Amplification Kit Product P/N 4322288 Insert P/N 4322638 REV G .

106. The User Manual for the AB Identifiler® Kit (Exhibit 61) indicates the components permit "accurate characterization of the alleles amplified," i.e. permitting one to determine the alleles present: "The AmpFlSTR Identifiler® Allelic Ladder was developed by Applied Biosystems for accurate characterization of the alleles amplified by the AmpFlSTR Identifiler® kit. The AmpFlSTR Identifiler® Allelic Ladder contains the majority of alleles reported for the 15 loci." *AmpFlSTR® Identifiler® PCR Amplification Kit User's Manual, Copyright 2006, 2010 Applied Biosystems, pg 3-32* [underlining added].

107. The User Manual for the AB Identifiler® Kit (Exhibit 61) indicates that the AB system permits detecting and evaluating amplified alleles: "A ±0.5-bp window allows for the detection and correct assignment of alleles. An allele that sizes only one base pair different from an allele in the allelic ladder will not be incorrectly typed and will be identified as off-ladder." *AmpFlSTR® Identifiler® PCR Amplification Kit User's Manual, Copyright 2006, 2010 Applied Biosystems, pg 4-8* [underlining added].

108. The Identifiler® Kit is identified in the User Manual (Exhibit 61) as containing sufficient reagents so as to permit many PCR amplifications: "The AmpFlSTR Identifiler kit contains sufficient quantities of the following reagents and the appropriate licenses to perform 200 25-µL amplifications …" *AmpFlSTR® Identifiler® PCR Amplification Kit User's Manual, Copyright 2006, 2010 Applied Biosystems* pg 1-7 [underlining added].

109. The User's Manual for the Identifiler® Kit (Exhibit 61) indicates that the control DNA can be amplified with the primers to generate many copies of the STR "alleles." *AmpFlSTR® Identifiler® PCR Amplification Kit User's Manual, Copyright 2006, 2010 Applied Biosystems (Figure3-6).*

110. The User's Manual for the Identifiler® Kit (Exhibit 61) illustrates results obtained when one has a sample with a mixture of DNA from two individuals. Figure 4-16 provides illustrative results when two samples are mixed at different ratios. There is a discussion of using quantitative analysis on these mixtures to determine which alleles are from the minor DNA contributor on page 4-41. Basically, the instrument quantitates the peak heights for each of the amplified alleles, allowing for a comparison of the relative amount of DNA corresponding to each allele. The amount of amplified DNA for an allele is an approximate indicator of the amount of sample DNA containing that allele. *AmpFlSTR® Identifiler® PCR Amplification Kit User's Manual, Copyright 2006, 2010 Applied Biosystems.*

111. The Product Insert for the Identifiler® Kit (Exhibit 60) identifies a size standard as "Required Materials – Not Included" and describes the size standard as follows:

> GeneScan™-500 LIZ® Size Standard 4322682 2 tubes each containing 200 µL of size standard. Loading buffer is included as a separate tube. GeneScan™-500 LIZ® Size Standard (not GeneScan™-350 ROX™ or GeneScan™-500 ROX™ Size Standards) must be used with the AmpFlSTR® Identifiler® kit.
>
> *AmpFlSTR® Identifiler® PCR Amplification Kit Product P/N 4322288 Insert P/N 4322638 REV G* [underlining added].

ABI/LT Profiler® Kit

112. The Product Insert for the AB Profiler® PCR Amplification Kit (Exhibit 62) lists "PCR Reaction Mix" (which contains the triphosphates in a PCR buffer), primer sets, AmpliTaq Gold® DNA Polymerase, and "Control DNA 9947A" among the components of the kit. A recommended range of "input sample DNA" is set forth. Clearly these are reagents for performing a PCR amplification reaction. While the control DNA is provided, the test DNA is not in the kit and is provided by the particular lab where the kit will be used. The primers will anneal to this test DNA as part of the PCR reaction. The kits are indicated as able to "amplify and type" in the context of an ABI PRISM machine. *AmpFlSTR® Profiler® PCR Amplification Kit, Product P/N 403038 Insert P/N 4304212 REV J.*

113. The Product Insert for the AB Profiler® PCR Amplification Kit (Exhibit 62) indicates that the kit includes dye-labeled primers for nine STR loci (plus a gender marker) in a single tube: "One tube of locus-specific 5-FAM-, JOE-, and NED-labeled and unlabeled primers in buffer to amplify the STR loci D3S1358, vWA, FGA, TH01, TPOX, CSF1PO, D5S818, D13S317, and D7S820, and the gender marker amelogenin. *AmpFlSTR® Profiler® PCR Amplification Kit, Product P/N 403038 Insert P/N 4304212 REV J.* All of the STRs amplified by this kit contain tetranucleotide repeats. *AmpFlSTR® Profiler® PCR Amplification Kit User's Manual Copyright 2006, 2010 Applied Biosystems, pg 9-16.*

114. The User's Manual for the AB Profiler® PCR Amplification Kit (Exhibit 63) indicates that the dyes are fluorescent dyes: "PCR-amplified STR alleles can be detected using various methods, such as fluorescent dye labeling …" *AmpFlSTR®*

Profiler® PCR Amplification Kit User's Manual Copyright 2006, 2010 Applied Biosystems, pg 1-1. (underlining added).

115. The User's Manual for the AB Profiler® PCR Amplification Kit (Exhibit 63) indicates that the kit employs allelic ladders to type the samples: "The AmpFlSTR® Allelic Ladders are used to genotype the analyzed samples. The alleles contained in the allelic ladders and the genotype of the AmpFlSTR® Control DNA 9947A are listed in Table 1-3." *AmpFlSTR® Profiler® PCR Amplification Kit User's Manual Copyright 2006, 2010 Applied Biosystems*, pg 1-8 [underlining added].

116. The User's Manual for the Profiler® PCR Amplification Kit (Exhibit 63) provides instructions for using the components of the kit to perform a multiplex polymerase chain reaction: "… protocols for PCR amplification of the AmpFlSTR Profiler loci." *AmpFlSTR® Profiler® PCR Amplification Kit User's Manual Copyright 2006, 2010 Applied Biosystems*, pg 1-4 [underlining added]

117. The User's Manual for the Profiler® PCR Amplification Kit (Exhibit 63) provides instructions for using the components of the kit to "co-amplify" STR loci: "The AmpFlSTR Profiler PCR Amplification Kit co-amplifies the repeat regions of the following nine short tandem repeat loci …" *AmpFlSTR® Profiler® PCR Amplification Kit User's Manual Copyright 2006, 2010 Applied Biosystems*, pg 1-5 [underlining added].

ABI COfiler® Kit

118. The Product Insert for the AB COfiler® Kit (Exhibit 64) indicates the kit contains "PCR Reaction Mix," dye-labeled primers, DNA polymerase, and "Control DNA

9947A." Clearly these are reagents for performing a PCR amplification reaction. A recommended range of "input sample DNA" is set forth. While the control DNA is provided, the test DNA is not in the kit and is provided by the particular lab where the kit will be used. The primers will anneal to this test DNA as part of the PCR reaction. The kits are indicated as able to "amplify and type" in the context of an ABI PRISM machine. *AmpFlSTR® COfiler® PCR Amplification Kit, Product P/N 4305246 Insert P/N 4305253 REV K.*

119. The User's Manual for the AB COfiler® Kit (Exhibit 65) indicates the kit "co-amplifies the repeat regions of the following six tetranucleotide short tandem repeat loci: D3S1358, D16S539, TH01, TPOX, CSF1PO, and D7S820." *AmpFlSTR® COfiler® PCR Amplification Kit User's Manual Copyright 2006, 2010 Applied Biosystems*, pg 1-5.

120. The User's Manual for the AB COfiler® Kit (Exhibit 17) indicates the kit is to be used "in conjunction with the AmpFlSTR® Profiler Plus™ PCR Amplification Kit to amplify the selected 13 STR loci in two PCR reactions." *AmpFlSTR® COfiler® PCR Amplification Kit User's Manual Copyright 2006, 2010 Applied Biosystems*, pg 1-1 (underlining added).

121. The User's Manual for the AB COfiler® Kit (Exhibit 17) indicates an allelic ladder is provided in the kit and that it "contains the most common alleles for each locus." *AmpFlSTR® COfiler® PCR Amplification Kit User's Manual Copyright 2006, 2010 Applied Biosystems*, pg 2-3.

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AB Profiler Plus® Kit

122. The User's Manual for the AB Profiler Plus® PCR Amplification Kit (Exhibit 66) lists "PCR Reaction Mix" (which contains the triphosphates in a PCR buffer), primer sets, AmpliTaq Gold® DNA Polymerase, and "Control DNA 9947A" among the components of the kit. (Table 1-2) A recommended range of "input sample DNA" is set forth. (p.1-9) Clearly these are reagents for performing a PCR amplification reaction. While the control DNA is provided, the test DNA is not in the kit and is provided by the particular lab where the kit will be used. The primers will anneal to this test DNA as part of the PCR reaction. The kits are indicated as able to "amplify and type" the recommended amount of sample DNA. (p. 12-10) *AmpFlSTR® Profiler Plus® PCR Amplification Kit User's Manual, Product* P/N 43033.

123. The User's Manual for the AB Profiler® PCR Amplification Kit (Exhibit 66) indicates that the kit includes dye-labeled primers for nine STR loci (plus a gender marker) in a single tube: "One tube of locus-specific 5-FAM-, JOE-, and NED-labeled and unlabeled primers in buffer to amplify the STR loci D3S1358, vWA, FGA, D8S1179, D21S11, D18S51, D5S818, D13S317, and D7S820, and the gender marker amelogenin." (Table 1-2) All of the STRs amplified by this kit contain tetranucleotide repeats. (Table 1-1)

124. The User's Manual for the AB Profiler Plus® PCR Amplification Kit (Exhibit 66) indicates that the dyes are fluorescent dyes: "The fluorescent dyes attached to the primers are light-sensitive." (p. 5-2)

125. The User's Manual for the AB Profiler Plus® PCR Amplification Kit (Exhibit 66) indicates that the kit employs three allelic ladders to type the samples: "The AmpFlSTR Allelic Ladders are used to genotype the analyzed samples. The alleles contained in the allelic ladders and the genotype of the AmpFlSTR Control DNA 9947A are listed in Table 1-3." [underlining added]

126. The User's Manual for the Profiler Plus® PCR Amplification Kit (Exhibit 66) provides instructions for using the components of the kit to perform a multiplex polymerase chain reaction in the protocol starting on page 5-2.

127. The User's Manual for the Profiler Plus® PCR Amplification Kit (Exhibit 66) provides instructions for using the components of the kit to "co-amplify" STR loci: "The AmpFlSTR Profiler Plus PCR Amplification Kit contains the PCR reagents necessary to co-amplify the ten AmpFlSTR Profiler Plus loci." (p. 1-7)

AB Yfiler® Kit

128. The Product Insert for the AB Yfiler® Kit (Exhibit 67) lists "PCR Reaction Mix" (with dNTPs in a PCR buffer), dye-labeled primer sets, AmpliTaq Gold DNA Polymerase, and "Control DNA 007." Clearly these are reagents for performing a PCR amplification reaction. While the control DNA is provided, the test DNA is not in the kit and is provided by the particular lab where the kit will be used. The primers will anneal to this test DNA as part of the PCR reaction. The kits are indicated as able to "amplify and type" in the context of an ABI PRISM machine. *AmpFlSTR® Yfiler® PCR Amplification Kit, Product P/N 4359513 Insert P/N 4359563 REV G.*

129. The Product Insert for the Yfiler® PCR Amplification Kit (Exhibit 67) indicates that the kit amplifies 15 STR loci found on the human Y chromosome. *AmpFlSTR® Yfiler® PCR Amplification Kit, Product P/N 4359513 Insert P/N 4359563 REV G*

130. The User's Manual for the Yfiler® PCR Amplification Kit (Exhibit 68) indicates that loci have repeat sequences of 3 to 6 bases that are tandemly repeated. For example, it indicates that the DYS385 14.2 allele contains 14 complete four base pair repeat units and a partial repeat unit of two base pairs. *AmpFlSTR® Yfiler® PCR Amplification Kit User's Manual Copyright 2006, 2010 Applied Biosystems*, pg 5-53.

131. The User's Manual for the Yfiler® PCR Amplification Kit (Exhibit 68) indicates the alleles, and these include both simple and cryptically simple DNA sequences. For example, DYS458 contains simple DNA sequence repeats of $[GAAA]_{13}$ to $[GAAA]_{20}$ (http://www.cstl.nist.gov/strbase/str_y458.) *AmpFlSTR® Yfiler® PCR Amplification Kit User's Manual Copyright 2006, 2010 Applied Biosystems*, p. 6-26.

132. Below, I identify the technical elements in the kit claims (section D) and method claims (section E) and find them in the accused products.

D. The Accused Products Have The Technical Elements Specified in the Kit Claims

133. I understand that there is a dispute between the parties concerning whether the claims of the asserted Promega Patents, which require the amplification of certain identified loci in the required multiplex reaction, are or are not open-ended, i.e. whether or not primers for additional loci not identified in such claims may also be present in the multiplex reaction. For purposes of this report, I have been

asked to assume that such claims are open-ended and that additional loci not identified in such claims may be amplified in the multiplex reaction.

Claim 42 of the '984 Patent

134. I understand that Promega is asserting that a number of claims of the RE37,984 Patent are infringed by Life Tech/AB when certain products are sold outside the licensed fields. Claim 42 is a kit claim which specifies five (5) elements:

A. a vessel comprising a mixture of primers,

B. a vessel containing a polymerase,

C. a vessel containing triphosphates,

D. a vessel containing a buffer for performing PCR and

E. a vessel containing control template DNA comprising i) simple or cryptically simple repeats, the repeat motif of 3 to 10 nucleotides in length and ii) flanking sequences for annealing at least one pair of primers.

All of the accused products provide these reagents. As noted above (paragraph 96), the Insert for the Identifiler® Kit lists "PCR Reaction Mix" (which contains the triphosphates in a buffer solution to support PCR satisfying components c) and d)), along with a) primer sets to amplify STR loci, b) AmpliTaq Gold® DNA Polymerase, and e) control DNA. As noted above, the COfiler® Kit (see paragraph 118), Profiler Plus® (paragraph122) and Yfiler® Kit (paragraph128) contain these components. The Profiler® Kit also contains these reagents (paragraph 112). To the extent the triphosphates and buffer in these kits are not in

separate vessels, there is no significant technical difference, since they will all eventually be mixed together in the PCR reaction.

135. Part e) of Claim 42 of the '984 Patent indicates that the template DNA in the kit must be such that repeats of 3 to 10 nucleotides in length can be amplified with the primers in the kit (although no specific loci are mentioned in Claim 42). As noted above, the accused AB/LT kits contain control DNA template which the primers can amplify. More specifically, as noted above (paragraph 109), the User's Manual for the Identifiler® Kit (Exhibit 61) indicates that the control DNA can be amplified with the primers to generate "alleles."

136. Part e) of Claim 42 specifies repeats and repeat "motifs" (a term I explained above, at paragraph 78). All of the accused products amplify a locus which has either simple or cryptically simple sequence repeats. For example, the COfiler® Kit includes the TPOX locus among the loci amplified. The TPOX locus has many alleles which are simple $(AATG)_n$ repeats. In addition, the Identifiler® Kit and the Profiler Plus® Kit include the D21S11 locus among the loci amplified (as noted previously at paragraph 95, all of the alleles at this locus are cryptically simple repeats of various types). The Identifier® Kit, the Profiler® Kit, and the Profiler Plus® Kit include the D5S818 locus among the loci amplified (as noted previously at paragraph 95, all of the alleles with sequences shown are simple repeats). The alleles amplified by the Yfiler® PCR Amplification Kit have repeat sequences of 3 to 6 bases that are tandemly repeated (paragraph 130); the alleles include both simple and cryptically simple DNA sequences (see paragraph 131, above). All of the STRs amplified by the kits described above consist of simple

or cryptically simple DNA repeats of 3-6 nucleotides. Therefore, I conclude that the accused products provide the technical elements set forth in Claim 42 of the '984 Patent.

Claim 5 of the '771 Patent

137. I understand that the only asserted Claim of U.S. Patent No. 7,008,771 is Claim 5 and that Promega asserts this claim is directly infringed by the Life Tech/AB Identifiler® product (when sold outside the licensed fields). Claim 5 is a kit claim which recites in part: "A kit for simultaneously analyzing a set of loci of genomic DNA, comprising oligonucleotide primers for co-amplifying a set of loci of the Genomic DNA to be analyzed, wherein the primers are in one or more containers, wherein the primers are designed to co-amplify a set of loci from one or more DNA samples, comprising short tandem repeat loci . . . [list of 13 particular loci] and a locus selected from the group consisting of G475 . . .and Amelogenin." (Claim 5, underlining added).

138. I have looked at the technical elements specified in Claim 5. Claim 5 specifies 13 particular loci (along with an additional locus which can be Amelogenin) to be co-amplified. The Life Tech/AB Identifiler® product is indicated to be a "Fluorescent STR kit" that includes, among other things, primers for co-amplifying "15 STR loci" which include the 13 recited STR loci in Claim 5 and the Amelogenin locus (see paragraphs 102-103, above). Therefore, I conclude that the accused product provides the technical elements set forth in Claim 5 of the '771 Patent.

139. So that there is no confusion, I note that, while Claim 5 specifies "HUMCSF1PO," HUMTH01," and "HUMTPOX," these loci are also known simply as CSF1PO, TH01 and TPOX. While Claim 5 specifies "HUMFIBRA," this locus is also known simply as FGA. While Claim 5 specifies HUMvWFA31," this locus is also known simply as vWA. The AB kits use the shorter name for these loci.

Claims 18-19 and 21-23 of the '235 Patent

140. I understand that Promega asserts that Claims 1, 4, 6-13, 15-19, and 21-23 of U.S. Patent No. 6,479,235 are directly infringed by the Life Tech/AB Identifiler® product when sold outside the licensed fields. I have looked at the technical elements specified in these claims. Claim 18 is a kit claim which recites in part: "A kit for simultaneously analyzing a set of loci of genomic DNA comprising oligonucleotide primers for co-amplifying a set of loci of the genomic DNA to be analyzed, wherein the set of loci comprises short tandem repeat loci which can be co-amplified, the primers are in one or more containers, the genomic DNA is human genomic DNA, and the loci comprise . . . . [list of 13 particular loci]. (Claim 18, underlining added). Claim 18 specifies 13 particular loci to be co-amplified. The Life Tech/AB Identifiler® product is indicated to be a "Fluorescent STR kit" that includes, among other things, primers for co-amplifying "15 STR loci" which include the 13 required STR loci in Claim 18 plus amelogenin (see paragraphs 102-103). Therefore, I conclude that the accused product provides the technical elements set forth in Claim 18 of the '235 Patent.

141. So that there is no confusion, I again note that, while Claim 18 specifies "HUMCSF1PO," HUMTH01," and "HUMTPOX," these loci are also known simply as CSF1PO, TH01 and TPOX. While Claim 18 specifies "HUMFIBRA," this locus is also known simply as FGA. While Claim 18 specifies HUMvWFA31," this locus is also known simply as vWA. The AB kit refers to the short name for these loci.

142. Claim 19 of the '235 Patent depends on Claim 18 and adds the feature that all of the primers are in one container. As noted previously, the primers in the Identifiler® product kit are in "one tube" (paragraph 102, above). Therefore, I conclude that the accused product provides the technical elements set forth in Claim 19 of the '235 Patent.

143. Claim 21 of the '235 Patent depends on Claim 18 and adds the feature of "reagents for at least one multiplex amplification reaction." Such reagents would include a polymerase and triphosphates. As noted above (paragraphs 96, 99-101), the Identifiler® Kit contains such reagents. Therefore, I conclude that the accused product provides the technical elements set forth in Claim 21 of the '235 Patent.

144. Claim 22 of the '235 Patent depends on Claim 18 and adds the feature of an "allelic ladder." The Identifiler® Kit also specifies an "Allelic Ladder" (see paragraph 105, above). Therefore, I conclude that the accused product provides the technical elements set forth in Claim 22 of the '235 Patent.

145. Claim 23 of the '235 Patent depends on Claim 22 and adds the feature that the rungs of the allelic ladder and at least one primer have a fluorescent label covalently attached, and at least two primers have different labels. The Identifier®

Kit provides allelic ladder rungs and primers that are covalently labeled with fluorescent dyes, including primers with different labels (see paragraphs 102-103, 105, above). Therefore, I conclude that the accused product provides the technical elements set forth in Claim 23 of the '235 Patent.

Claim 25 and 27-31 of the '660 Patent

146. I understand that Promega asserts that Claims 2-5, 9, 16-17, 19-21, 23-25, and 27-31 of U.S. Patent No. 5,843,660 are directly infringed by the Life Tech/AB Identifiler® product when sold outside the licensed fields. I have looked at the technical elements specified in these claims. Claim 25 is a kit claim which recites in part: "A kit for simultaneously analyzing short tandem repeat sequences in at least three loci, comprising a container which has oligonucleotide primers for co-amplifying a set of at least three short tandem repeat loci, wherein the set of loci are selected from the sets of loci consisting of: [list of 29 sets of loci]. (Claim 25, underlining added). While 29 sets of loci are set forth in Claim 25, one of the 29 sets specifies that the three loci are D16S539, D7S820, and D13S317. As noted above, the Identifiler® Kit contains primers in a single tube (paragraph 102) to co-amplify loci combinations including D7S820, D13S317, and D16S539. Therefore, I conclude that the accused product provides the technical elements set forth in Claim 25 of the '660 Patent.

147. Claim 27 depends on Claim 25 and further specifies "a container having reagents for at least one multiplex amplification reaction." As noted above, the Identifiler® Kit provides multiplex amplification reaction reagents (paragraph 96, 99-101).

Therefore, I conclude that the accused product provides the technical elements set forth in Claim 27 of the '660 Patent.

148. Claim 28 depends on Claim 25 and further specifies "a container having an allelic ladder." As noted previously, the Identifiler® Kit provides a container having an allelic ladder (paragraph 105). Therefore, I conclude that the accused product provides the technical elements set forth in Claim 28 of the '660 Patent.

149. Claim 29 depends on Claim 28 and further specifies "each rung of the allelic ladder and at least one primer … have a label covalently attached." As noted previously, the Identifiler® Kit provides allelic ladder rungs and primers that are covalently labeled (see paragraphs 102-105, above). Therefore, I conclude that the accused product provides the technical elements set forth in Claim 29 of the '660 Patent.

150. Claim 30 depends on Claim 29 and further specifies "the label is a fluorescent label." As noted previously, the Identifiler® Kit provides reagents with fluorescent labels (see paragraph 103). Therefore, I conclude that the accused product provides the technical elements set forth in Claim 30 of the '660 Patent.

151. Claim 31 depends on Claim 30 and further specifies "at least one of the … primers … has a different fluorescent label …". As noted previously, the Identifier® Kit provides at least one primer fluorescent label that is different from another primer fluorescent label (see paragraphs 102-105). Therefore, I conclude that the accused product provides the technical elements set forth in Claim 31 of the '660 Patent.

Claims 10, 23-24, 27 and 33 of the '598 Patent

152. I understand that Promega asserts that Claims 1-2, 4-10, 12, 15, 19, 21-24, 27-28, and 31-33 of U.S. Patent No. 6,221,598 are directly infringed by some ABI products, including the Life Tech/ABI Identifiler® product and Profiler® Kit when sold outside the licensed fields. I have looked at the technical elements specified in these claims. Claim 10 is a kit claim which recites in part: "A kit for simultaneously analyzing short tandem repeat sequences in at least three loci, comprising: a single container containing oligonucleotide primers for each locus in a set of at least three short tandem repeat loci, wherein the at least three short tandem repeat loci in the set comprises at least three loci selected from the group consisting of: [list of 20 sets of loci]. (Claim 10, underlining added). While 20 different sets of loci are listed in Claim 10, one set specifies that the loci include at least HUMTPOX, HUMVWFA31 and HUMCSF1PO (in a first case), and (in another case) HUMCSF1PO, HUMTH01 and HUMVWFA31 (among a number of possible sets). As noted previously, simpler names for these loci are TPOX, vWA and CSF1PO (in the one case) and CSF1PO, TH01 and vWA (in the other). The Identifiler® Kit and the Profiler® Kit provide a single container with primers for these two combinations of three loci (as well as additional loci) (see paragraphs 102 and 113). Therefore, I conclude that the Identifiler® Kit and the Profiler® Kit provide the technical elements set forth in Claim 10 of the '598 Patent.

153. Claim 23 of the '598 Patent is also a kit claim which specifies in part: "A kit for simultaneously analyzing short tandem repeat sequences in a set of short tandem

repeat loci from one or more DNA samples, comprising: a single container containing oligonucleotide primers for each locus in a set of short tandem repeat loci which can be co-amplified, comprising, HUMCSF1PO, HUMTPOX and HUMTH01." (Claim 23, underlining added). Claim 23 indicates the loci include HUMCSF1PO, HUMTPOX, and HUMTH01 (or more simply, CSF1PO, TPOX and TH01). The COfiler® Kit co-amplifies TPOX, TH01 and CSF1PO (along with other loci) which are the loci specified in Claim 23 (see paragraph 119). The Identifiler® Kit and the Profiler® Kit provide a single container with primers for these three loci (as well as additional loci) (see paragraphs 102 and 113). Therefore, I conclude that the Identifiler® Kit, COfiler® Kit and the Profiler® Kit provide the technical elements set forth in Claim 23 of the '598 Patent.

154. Claim 24 depends on Claim 23 and further specifies that the kit contains primers designed to co-amplify the HUMVWFA31 (or more simply vWA) locus. The Identifiler® Kit (see paragraph 102) and the Profiler® Kit (see paragraph 113) are identified as providing a single container with primers for this locus as well. Therefore, I conclude that the Identifiler® Kit and the Profiler® Kit provide the technical elements set forth in Claim 24 of the '598 Patent.

155. Claim 27 depends on Claim 23 and specifies "at least one of each of the pair of oligonucleotide primers in the kit is fluorescently-labeled." As noted previously, the Identifiler® Kit (see paragraphs 102-103), COfiler® Kit (see paragraph 119) and the Profiler® Kit (see paragraphs 113-114) are identified as providing fluorescently labeled primers. Therefore, I conclude that the Identifiler® Kit,

COfiler® Kit and the Profiler® Kit provide the technical elements set forth in Claim 27 of the '598 Patent.

156. Claim 33 is another independent kit claim of the '598 Patent and it recites in part: "A kit for simultaneously analyzing short tandem repeat sequences in a set of short tandem repeat loci from one or more DNA samples, comprising: a single container containing oligonucleotide primers for each locus in a set of short tandem repeat loci which can be co-amplified, comprising, HUMTPOX, HUMVWFA31, and HUMCSF1PO." (Claim 33, underlining added). Claim 33 indicates that the loci include HUMCSF1PO, HUMTPOX and HUMVWFA31 (or more simply, CSF1PO, TPOX and vWA). The Identifiler® Kit (see paragraph 102) and the Profiler® Kit (see paragraph 113) are identified as providing a single primer container for these loci. Therefore, I conclude that the Identifiler® Kit and the Profiler® Kit provide the technical elements set forth in Claim 33 of the '598 Patent.

E. The Accused Products Have The Technical Elements Specified in the Method Claims

Claims 15-16, 18, 23, 25, 27-28 and 41 of the '984 Patent

157. I understand that Promega is asserting that a number of method claims of the RE37,984 Patent are infringed by Life Tech/AB when certain products are sold outside the licensed fields. Claim 15 is a method claim which recites in part: "A method for analyzing length polymorphisms in at least one locus in an DNA sample . . . wherein said DNA sample comprises a DNA template having at least

one locus comprising a simple or cryptically simple DNA sequence, said method comprising:

A. annealing said DNA template with at least one pair of primers, wherein said primer pair is composed of a first primer complementary to a nucleotide sequence flanking said simple or cryptically simple DNA sequence on the 5' side of said simple or cryptically simple DNA sequence and a second primer complementary to a nucleotide sequence flanking the simple or cryptically simple DNA sequence on the 3' side of said simple or cryptically simple DNA sequence; wherein said first and second primers each anneal to a single site in said DNA template and wherein the annealing sites are separated by 50 to 500 nucleotides of template DNA;

B. performing at least one primer-directed polymerase chain reaction upon said template DNA having said primers annealed thereto, so as to form at least one polymerase chain reaction product;

C. separating the products of each polymerase chain reaction according to their lengths; and

d) analyzing the lengths of the separated products to determine the length polymorphisms of said simple or cryptically simple sequences;

wherein said simple or cryptically simple sequence has a repeat length of 3 to 10 nucleotides.

I have discussed the meaning of "simple" and "cryptically simple sequences" shown underlined above (see paragraphs 93-95). As noted above in the context of Claim 42 of the '984 Patent, all of the accused products amplify a locus which has either simple or cryptically simple sequence repeats. For example, the COfiler® Kit includes the TPOX locus among the loci amplified. The TPOX locus has many alleles which are simple $(AATG)_n$ repeats. In addition, the Identifiler® Kit and the Profiler Plus® Kit include the D21S11 locus among the loci amplified (as noted previously at paragraph 95, all of the alleles at this locus are cryptically simple repeats of various types). The Identifier® Kit, the Profiler® Kit, and the Profiler Plus® Kit include the D5S818 locus among the loci amplified (as noted previously at paragraph 95, all of the alleles with sequences shown are simple repeats). The alleles amplified by the Yfiler® PCR Amplification Kit have repeat sequences of 3 to 6 bases that are tandemly repeated; the alleles include both simple and cryptically simple DNA sequences (see paragraphs 129-130, above).

158. I have also discussed the steps of a) annealing and b) performing a PCR reaction, (see underlining in Claim 15 above) in general terms previously (see paragraphs 79-83). These steps are specified for users of the accused kits. For example, the COfiler® Kit is a PCR amplification kit with primers for annealing, as part of the PCR reaction (see paragraphs 118-119). Similarly, the Identifiler® Kit (paragraph 96), Profiler® Kit (paragraph 112), and the Profiler Plus® Kit (paragraph 122) provide reagents for PCR, including primers for annealing to

template as part of the PCR reaction. Finally, the Yfiler® Kit is a PCR amplification kit with primers for annealing, as part of the PCR reaction (see paragraph 128). Figure 3-6 of the Identifiler Users Manual shows that the allele sizes of the amplified STRs range from about 107 to 340 nucleotides in length meaning that the primer annealing sites are separated by slightly less than that distance. Similarly Figure 5-3 of the Yfiler User's Manual (Exhibit 68) demonstrates that the allele sizes range from about 100 to 330 nucleotides in length.

159. I have also discussed the steps of c) separating the PCR products, and d) analyzing the separated products to determine length polymorphisms which are underlined above in Claim 15 (see paragraphs 86, 89-91). These steps are specified for users of the accused kits. For example, the COfiler® Kit is a PCR amplification kit which is indicated as able to "amplify and type" in the context of an ABI PRISM machine (see paragraph 118). The Yfiler® Kit is a PCR amplification kit which is indicated as able to "amplify and type" in the context of an ABI PRISM machine (see paragraph 128). Similarly, the Identifiler® Kit (paragraph 96), Profiler® Kit (paragraph 112) and the Profiler Plus® Kit (paragraph 122) are indicated as able to "amplify and type" in the context of an ABI PRISM machine. The User Guide for the Identifiler® Kit indicates that the PCR products are "electrophoretically separated" and "detected" on the ABI PRISM instrument. Therefore, I conclude that the Identifiler® Kit, the Profiler® Kit, the Profiler Plus® Kit, the Yfiler® Kit, and the COfiler® Kit all provide the technical elements set forth in Claim 15 of the '984 Patent.

160. Claim 16 of the '984 Patent depends on Claim 15 and further specifies that the repeat length is between 3 and 6 nucleotides. I discussed repeat lengths of the loci amplified by the kits in the context of the length range of 3 to 10 nucleotides for Claim 15 (see paragraph 157). Claim 16 simply is a narrower range. Nonetheless, the kits amplify loci with repeat lengths in this range. For example, as noted previously, the alleles amplified by the Yfiler® PCR Amplification Kit have repeat sequences of 3 to 6 bases that are tandemly repeated; the alleles include both simple and cryptically simple DNA sequences (see paragraphs 129-130, above). Therefore, I conclude that the Identifiler® Kit, the Profiler® Kit, the Profiler Plus® Kit, the Yfiler® Kit, and the COfiler® Kit all provide the technical elements set forth in Claim 16 of the '984 Patent.

161. Claim 18 of the '984 Patent depends on Claim 15 and further specifies that "at least two primer pairs are used." As noted previously, the accused kits have many primer pairs for amplification of many loci (see paragraphs 96, 102, 112-113, 118-119, 122-123, 128-129, above). Therefore, I conclude that the Identifiler® Kit, the Profiler® Kit, the Profiler Plus® Kit, the Yfiler® Kit, and the COfiler® Kit all provide the technical elements set forth in Claim 18 of the '984 Patent.

162. Claim 23 of the '984 Patent depends on Claim 15 and further specifies that "2 to 50 primer pairs are used." As noted previously, the accused kits have primer pairs for amplification of loci, the number of which falls within this range (see paragraphs 96, 102, 112-113, 118-119, 122-123, 128-129, above). Therefore, I conclude that the Identifiler® Kit, the Profiler® Kit, the Profiler Plus® Kit, the

Yfiler® Kit, and the COfiler® Kit all provide the technical elements set forth in Claim 23 of the '984 Patent.

163. Claim 25 depends on Claim 15 and further specifies that "each of the products of the primer-directed polymerase chain reaction is separable one from the other as individual bands on a suitable electrophoretic gel." As noted above, each of the accused products is able to amplify and type in the context of an ABI PRISM instrument (see paragraphs 96, 112, 118, 122 and 128) and this instrument is used to "electrophoretically separate" and "detect" the amplified products using a "five-dye fluorescent system" (see paragraph 103-104). Thus, size and color signal are used together to separate "one from the other." Therefore, I conclude that the Identifiler® Kit, the Profiler® Kit, the Profiler Plus® Kit, the Yfiler® Kit, and the COfiler® Kit all provide the technical elements set forth in Claim 25 of the '984 Patent.

164. Claim 27 depends on Claim 15 and specifies that the PCR product "is labeled by a non-radioactive label." As noted above, each of the accused products utilizes dye-labeled primers (see paragraphs 102, 113-114, 119, 124, 128-129), which will generate a PCR product labeled with a non-radioactive label. Therefore, I conclude that the Identifiler® Kit, the Profiler® Kit, the Profiler Plus® Kit, the Yfiler® Kit, and the COfiler® Kit all provide the technical elements set forth in Claim 27 of the '984 Patent.

165. Claim 28 depends on Claim 27 and specifies that the "non-radioactive label is a fluorescent label." As noted above, each of the accused products utilizes dye-labeled primers (see paragraphs 102, 113-114, 119, 124, 128-129). Moreover,

these dyes are fluorescent (see paragraphs 103 and 114). Therefore, I conclude that the Identifiler® Kit, the Profiler® Kit, the Profiler Plus® Kit, the Yfiler® Kit, and the COfiler® Kit all provide the technical elements set forth in Claim 28 of the '984 Patent.

166. Claim 41 of the '984 Patent is a method claim which recites in part: "A method for analyzing polymorphism in at least one locus in an DNA sample comprising a DNA template, said method comprising:

A. annealing said DNA template with at least one pair of primers, . . .

B. performing at least one primer-directed polymerase chain reaction upon said template DNA having said primers annealed thereto, so as to form at least one polymerase chain reaction product;

C. separating the products of each polymerase chain reaction product according to their lengths; and

D. analyzing the lengths of the separated products to determine the length polymorphisms of said simple or cryptically simple sequences, wherein said DNA template includes at least one sequence consisting essentially of a simple or cryptically simple DNA sequence having a repeat motif length of 3 to 10 nucleotides and nucleotide sequences flanking said simple or cryptically simple DNA sequence effective for annealing said at least one pair of primers."

I have discussed the meaning of "simple" and "cryptically simple sequences" shown underlined above (see paragraphs 93-95). As noted above in the context of Claim 42 of the '984 Patent, all of the accused products amplify a locus which has either simple or cryptically simple sequence repeats. For example, the COfiler® Kit includes the TPOX locus among the loci amplified. The TPOX locus has many alleles which are simple $(AATG)_n$ repeats. In addition, the Identifiler® Kit and the Profiler Plus® Kit include the D21S11 locus among the loci amplified (as noted previously at paragraph 95, all of the alleles at this locus are cryptically simple repeats of various types). The Identifier® Kit, the Profiler® Kit, and the Profiler Plus® Kit include the D5S818 locus among the loci amplified (as noted previously at paragraph 95, all of the alleles with sequences shown are simple repeats). The alleles amplified by the Yfiler® PCR Amplification Kit have repeat sequences of 3 to 6 bases that are tandemly repeated; the alleles include both simple and cryptically simple DNA sequences (see paragraphs 130, above). All of the other kits analyze STRs with tetranucleotide repeats (see paragraphs 102-113).

167. I have also discussed the steps of a) annealing and b) performing a PCR reaction, (see underlining in Claim 41 above) in general terms previously (see paragraphs 79-83). These steps are specified for users of the accused kits. For example, the COfiler® Kit is a PCR amplification kit with primers for annealing, as part of the PCR reaction (see paragraph 118). Similarly, the Identifiler® Kit (paragraph 96), Profiler® Kit (paragraph 112) and the Profiler Plus® Kit (paragraph 122) provide reagents for PCR, including primers for annealing to template as part of the PCR

reaction. Finally, the Yfiler® Kit is a PCR amplification kit with primers for annealing, as part of the PCR reaction (see paragraph 128).

168. I have also discussed the steps of c) separating the PCR products, and d) analyzing the separated products to determine length polymorphisms which are underlined above in Claim 41 (see paragraphs 86, 89-91). These steps are specified for users of the accused kits. For example, the COfiler® Kit is a PCR amplification kit which is indicated as able to "amplify and type" in the context of an ABI PRISM machine (see paragraph 118). The Yfiler® Kit is a PCR amplification kit which is indicated as able to "amplify and type" in the context of an ABI PRISM machine (see paragraph 128). Similarly, the Identifiler® Kit (paragraph 96), Profiler® Kit (paragraph 112) and the Profiler Plus® Kit (paragraph 122) are indicated as able to "amplify and type" in the context of an ABI PRISM machine. The User Guide for the Identifiler® Kit indicates that the PCR products are "electrophoretically separated" and "detected" on the ABI PRISM instrument (paragraph 104). Therefore, I conclude that the Identifiler® Kit, the Profiler® Kit, the Profiler Plus® Kit, the Yfiler® Kit, and the COfiler® Kit all provide the technical elements set forth in Claim 41 of the '984 Patent.

Claims 1, 12 and 28 of the '598 Patent (and dependent claims)

169. Claims 1, 12, and 28 are independent method claims of the '598 Patent. Claim 1 recites in part a method having the following steps:

A. obtaining at least one DNA sample to be analyzed;

B. selecting a set of at least three short tandem repeat loci of the DNA sample to be analyzed which can be co-amplified, wherein the at least three short tandem repeat loci in the set comprises at least three loci selected from the group consisting of: [list of 18 sets of loci];

C. co-amplifying . . . thereby producing a mixture of amplified alleles . . .; and

D. evaluating the amplified alleles . . . to determine the alleles present at each of the co-amplified loci in the set.

Claim 12 is similar to Claim 1, but differs in that it only sets forth a single set of loci.

Claim 12 recites in part:

a) obtaining at least one DNA sample to be analyzed;

b) selecting a set of short tandem repeat loci of the DNA sample to be analyzed which can be co-amplified, comprising HUMCSF1PO, HUMTPOX, and HUMTH01;

c) co-amplifying the set of short tandem repeat loci in a multiplex amplification reaction, thereby producing a mixture of amplified alleles from each of the co-amplified loci in the set; and

d) evaluating the amplified alleles in the mixture to determine the alleles present at each of the co-amplified loci in the set.

Claim 28 is similar to Claim 12 in that it also sets forth only a single set of loci. Claim 28 recites in part:

a) obtaining at least one DNA sample to be analyzed;

b) selecting a set of short tandem repeat loci of the DNA sample to be analyzed which can be co-amplified, comprising HUMTPOX, HUMVWFA31, and HUMCSF1PO;

c) co-amplifying the set of short tandem repeat loci in a multiplex amplification reaction, thereby producing a mixture of amplified alleles from each of the co-amplified loci in the set; and

d) evaluating the amplified alleles in the mixture to determine the alleles present at each of the co-amplified loci in the set.

170. From the above, it is clear that Claims 1, 12 and 28 have some common steps with some language in common (which is underlined above):

Step a)

Claims 1, 12, 28 at step a) specify "obtaining at least one DNA sample." All products accused of infringing the '598 Patent utilize at least one DNA sample in their protocols. Indeed, the Identifiler® Kit, the Profiler® Kit, and the COfiler® Kit all provide a recommended range of "input sample DNA." (paragraphs 97, 112, and 118 above). Therefore, I conclude that the technical elements for step a) of these claims are found in the accused kits.

Step b)

Claims 1, 12 and 28 specify at step b) "selecting a set of . . . short tandem repeat loci … which can be co-amplified." Specifically, claim 1 specifies in step

b) that the "at least three loci selected" are from a group which includes in one case HUMTPOX, HUMTH01, and HUMVWFA31, and in another case HUMCSF1PO, HUMTH01, and HUMVWFA31 (among a number of possible sets of loci listed). Claim 12 specifies in step b) that the set of loci selected comprises HUMCSF1PO, HUMTPOX, and HUMTH01. Claim 28 specifies in step b) that the set of loci selected comprises HUMTPOX, HUMVWFA31, and HUMCSF1PO. All products accused of infringing the '598 Patent utilize at least three short tandem repeat loci which can be co-amplified in their protocols. The COfiler® Kit co-amplifies TPOX, TH01 and CSF1PO (along with other loci), which is the precise combination specified in Claim 12. The Identifiler® Kit (paragraph 100) and the Profiler® Kit (paragraph 117) are identified as co-amplifying short tandem repeat loci which include all the sets of loci found in claims 1, 12, and 28. Therefore, I conclude that the technical elements for step b) of these claims are found in the accused kits.

Step c)

Claims 1, 12 and 28 further specify at step c) "co-amplifying . . . , thereby producing a mixture of amplified alleles . . ." I have discussed the meaning of amplifying and "co-amplifying" (see paragraphs 79-80, above). I have also noted that the Identifiler® Kit (see paragraphs 99-101), the COfiler® Kit (paragraph 119), and the Profiler® Kit (paragraph 117) all "co-amplify" to produce a mixture of alleles. Therefore, I conclude that

the technical elements for step c) of these claims are found in the accused kits.

Step d)

Claims 1, 12 and 28 further specify at step d) evaluating the amplified alleles . . . to determine the alleles present . . .” I have previously indicated that the Identifiler® Kit (see paragraph 96), the COfiler® Kit (paragraph 118), and the Profiler® Kit (paragraph 122) are able to “amplify and type” in the context of an ABI PRISM machine and thereby accurately characterize the alleles present (paragraph 104, 106-107). Therefore, I conclude that the technical elements for step d) of these claims are found in the accused kits.

171. Claim 2 of the ‘598 depends on Claim 1 and specifies that the loci “are co-amplified by multiplex polymerase chain reaction.” I have discussed the difference between “monoplex” (paragraph 84) and multiplex (paragraph 85) PCR reactions. The User Manual for the ABI Identifiler® Kit (Exhibit 61) makes this distinction (paragraph 101). I have previously indicated that the Identifiler® Kit (see paragraph 96), the COfiler® Kit (paragraph 118-119), and the Profiler® Kit (paragraph 116-117) provide reagents for performing a multiplex PCR amplification reaction. Therefore, I conclude that the technical elements for Claim 2 of the ‘598 are found in the accused kits.

172. Claim 4 of the ‘598 depends on Claim 1 and specifies that the alleles are evaluated by comparing the alleles to a size standard or a locus-specific allelic ladder. I have previously indicated that the Identifiler® Kit (see paragraph 105), the COfiler® Kit (paragraph 121), and the Profiler® Kit (paragraph 115) each

provide an allelic ladder including the most common alleles for each locus (i.e. it is locus specific). The kits also list a size standard as "required materials" (see e.g. paragraph 111). Page 3-22 of the Identifiler User Manual provides the protocol for preparing and analyzing amplified PCR products using both the size standard and the allelic ladder. The other kits are utilized in a similar fashion. Therefore, I conclude that the technical elements for Claim 4 of the '598 are found in the accused kits.

173. Claims 15 and 21 of the '598 specify that the set of loci co-amplified further comprises HUMVWFA31. I have noted previously that this locus is also known simply as vWA. The AB kits refer to the short name for this locus. The Identifiler® Kit (paragraph 102) and the Profiler® Kit (paragraph 113) also co-amplify this locus. Therefore, I conclude that the technical elements for Claims 15 and 21 of the '598 are found in the accused kits.

174. Claim 19 depends on Claim 12 and specifies "oligonucleotide primers for each locus in the set of loci selected in step (b), wherein at least one of the oligonucleotide primers for each locus is fluorescently labeled." The Identifiler® Kit (paragraphs 96, 102), COfiler® Kit (paragraphs 118-119) and the Profiler® Kit (paragraphs 112-113) provide oligonucleotide primers for each locus. The Identifiler® Kit (paragraph 102-103), COfiler® Kit (paragraph 119) and the Profiler® Kit (paragraph 114) indicate the primers are fluorescently labeled. Therefore, I conclude that the technical elements for Claim 19 of the '598 are found in the accused kits.

Claims of the 660 Patent

175. Claim 16 of the '660 is a method claim which reads in part: "comprising:

(a) obtaining at least one DNA sample to be analyzed,

(b) selecting a set of three short tandem repeat loci of the DNA sample to be analyzed which can be amplified together, wherein the set of three loci is selected from the group of sets of loci consisting of [six sets of loci];

(c) co-amplifying the three loci in the set in a multiplex amplification reaction, wherein the product of the reaction is a mixture of amplified alleles from each of the co-amplified loci in the set; and

(d) evaluating the amplified alleles in the mixture to determine the alleles present at each of the loci analyzed in the set within the DNA sample. Claim 1 (not asserted) of the '660 is similar except for the fact that it specifies "a set of at least four short tandem repeat loci."

176. Claims 2, 3, 4 and 5, each of which depends on Claim 1 (not asserted), and claim 16 each specify at step (a) "obtaining at least one DNA sample . . .". I have previously noted that the Identifiler® kit utilizes at least one DNA sample in its protocols. Indeed, the Identifiler® Kit provides a recommended range of "input sample DNA." (see paragraphs 97, above). Therefore, I conclude that the technical elements for step a) of these claims are found in the accused kit.

177. Claims 2, 3, 4 and 5 and 16 specify the following at step b):

> Claim 2: selecting "a set of at least four loci" from a "group of sets of loci" that include in one case "D7S820, D13S317, D16S539, HUMvWFA31."

Claim 3: selecting "a set of at least six loci" from a "group of sets of loci" that include in, one case, "D16S539, D7S820, D13S317, D5S818, HUMCSF1PO, and HUMTPOX."

Claim 4: selecting "a set of at least seven loci" from a "group of sets of loci" that include in, one case, "D16S539, D7S820, D13S317, D5S818, HUMCSF1PO, HUMTPOX, and HUMTH01."

Claim 5: selecting "a set of at least eight loci" from a "group of sets of loci" that include in, one case, "D16S539, D7S820, D13S317, D5S818, HUMCSF1PO, HUMTPOX, HUMTH01 and HUMvWFA31."

Claim 16: selecting "a set of at least three loci" from a "group of sets of loci" that include in, one case, "D16S539, D7S820, D13S317."

The Identifiler® Kit co-amplifies loci that include each of the above identified sets of loci regarding claims 2-5 and 16 (see paragraph 102, above). Therefore, I conclude that the technical elements for step b) of these claims are found in the accused kit.

178. Claims 2-5 and 16 further specify at step c) "co-amplifying . . ." I have discussed the meaning of amplifying and "co-amplifying" (see paragraphs 79-80, above). I have also noted that the Identifiler® Kit (see paragraphs 99-101) "co-amplifies" to produce a mixture of alleles. Therefore, I conclude that the technical elements for step c) of these claims are found in the accused kit.

179. Claims 2-5 and 16 further specify at step d) evaluating the amplified alleles . . . to determine the alleles present . . ." I have previously indicated that the Identifiler® Kit (see paragraph 96) is able to "amplify and type" in the context of an ABI PRISM machine and thereby accurately characterize the alleles present (paragraph 106). Therefore, I conclude that the technical elements for step d) of these claims are found in the accused kit.

180. Claim 17, which depends on claim 16, specifies that "the amplification is done using three pair of primers, wherein each pair of primers flanks one of the three

short tandem repeat loci." I have previously discussed the meaning of flanking regions (see paragraph 82 above). The Identifiler® Kit uses more than three primer pairs which flank the repeating sequence. Otherwise they could not amplify the STR loci they claim as referenced above.

181. Claim 19 depends on Claim 16 and specifies that "the multiplex reaction is a polymerase chain reaction". I have discussed the difference between "monoplex" (paragraph 84) and multiplex (paragraph 85) PCR reactions. The User Manual for the ABI Identifiler® Kit (Exhibit 61) makes this distinction (paragraph 101). I have previously indicated that the Identifiler® Kit (see paragraph 96) provides reagents for performing a multiplex PCR amplification reaction. Therefore, I conclude that the technical elements for Claim 19 of the '660 are found in the accused kit.

182. Claim 20 is dependent from Claim 16 and specifies "comparing separated alleles to a size standard, wherein the size standard is selected from a group of size standards consisting of a DNA marker and a locus-specific allelic ladder. " I have previously indicated that the Identifiler® Kit (see paragraph 105) provides an allelic ladder comprising the most common alleles for each locus (i.e. it is locus specific). The kits also list a size standard as "required materials" (see e.g. paragraph 111). The protocol included in the Identifiler® Kit User's Manual uses both to calculate the size of the amplified alleles and identify them. Therefore, I conclude that the technical elements for Claim 20 of the '660 are found in the accused kit.

Claims of the '235 Patent

183. Claims 1 and 13 of the '235 Patent are methods claims. Claim 1 of the '235 patent reads in part:

(a) obtaining at least one DNA sample to be analyzed,

(b) selecting a set of loci of the DNA sample, comprising D3S1358, D5S818, D7S820, D8S1179, D13S317, D16S539, D18S51, D21S11, HUMCSF1PO, HUMFIBRA, HUMTH01, HUMTPOX, and HUMvWFA31,

(c) co-amplifying the loci in the set in a multiplex amplification reaction, wherein the product of the reaction is a mixture of amplified alleles from each of the co-amplified loci in the set; and

(d) evaluating the amplified alleles in the mixture to determine the alleles present at each of the loci analyzed in the set within the DNA sample.

184. Claim 13 of the '235 Patent reads in part:

A. obtaining at least one DNA sample to be analyzed;

B. selecting a set of loci of the DNA sample, comprising short tandem repeat loci D3S1358, D5S818, D7S820, D8S1179, D13S317, D16S539, D18S51, D21S11, HUMCSF1PO, HUMFIBRA, HUMTH01, HUMTPOX, and HUMvWFA31;

C. co-amplifying the loci in the set in a multiplex amplification reaction, wherein the product of the reaction is a mixture of amplified alleles from each of the co-amplified loci in the set; and

D. evaluating the amplified alleles in the mixture to determine the alleles present at each of the loci analyzed in the set within the DNA sample.

185. With regard to step a) of Claim 1 and 13 of the '235 Patent, I have previously indicated that the Identifiler® Kit provides a recommended range of "input sample DNA." (see paragraphs 97, above). With regard to step b) of Claim 1 and 13 of the '235 Patent, I have previously indicated the Identifiler® Kit (paragraph 96 and 102) provides primers to amplify the loci of step b). With regard to step c) of Claim 1 and 13 of the '235 Patent, I have discussed the meaning of amplifying and "co-amplifying" (see paragraphs 79-80, above). I have also noted that the Identifiler® Kit (see paragraphs 99-101) "co-amplifies" to produce a mixture of alleles. With regard to step d) of Claim 1 and 13 of the '235 Patent, I have previously indicated that the Identifiler® Kit (see paragraph 96) is able to "amplify and type" in the context of an ABI PRISM machine and thereby accurately characterize the alleles present (paragraph 106). Therefore, I conclude that the technical elements for steps a) through d) of these claims are found in the accused kit.

186. Claim 4 depends on Claim 1 of the '235 Patent and specifies that the set of loci "further comprises a locus to identify the gender …". The Identifiler® Kit is identified as providing a gender identifying locus (paragraph 102). Therefore, I conclude that the technical elements for Claim 4 are found in the accused kit.

187. Claim 7 depends on Claim 1 and specifies "using pairs of oligonucleotide primers flanking the loci analyzed." As noted previously, the Identifiler® Kit uses primers

which flank the repeating sequence. Otherwise they could not amplify the STR loci they claim as referenced above. Therefore, I conclude that the technical elements for Claim 7 are found in the accused kit.

188. Claim 8 depends on Claim 7 and specifies that the set of loci "is co-amplified using a polymerase chain reaction". As noted above, the Identifiler® Kit is provides reagents to co-amplify loci using a "polymerase chain reaction" (paragraphs 96, 99-101). Therefore, I conclude that the technical elements for Claim 8 are found in the accused kit.

189. Claim 9 depends on Claim 7 and specifies that each locus is co-amplified "using a pair of primers which flank the locus wherein at least one primer of each pair has a fluorescent label covalently attached thereto." As noted above, the Identifiler® Kit, uses primers which flank the repeating sequence. Otherwise they could not amplify the STR loci they claim as referenced above. Moreover, I have previously noted that the primers are fluorescently labeled (paragraphs 102-103). Therefore, I conclude that the technical elements for Claim 9 are found in the accused kit.

190. Claim 10 depends on Claim 9 and specifies that "at least three" of the labeled primers have different fluorescent labels covalently attached thereto." The Identifiler® Kit is identified as providing that at least three primers are differentially labeled (see paragraphs 102-104). Therefore, I conclude that the technical elements for Claim 10 are found in the accused kit.

191. Claim 12 depends on Claim 1 and specifies that the amplified alleles are evaluated by comparing to "a size standard, wherein the size standard is selected

from a group of size standards consisting of a DNA marker and a locus specific allelic ladder. " I have noted previously that the Identifiler® Kit comes with an allelic ladder whose alleles are locus specific (paragraphs 105) and that a size standard is identified in the "required materials." (paragraph 111).

192. Claim 15 depends on Claim 13 and specifies that the multiplex amplification reaction "is a polymerase chain reaction." As noted above, the Identifiler® Kit provides reagents to co-amplify loci using a "polymerase chain reaction" (paragraphs 96, 99-101). Therefore, I conclude that the technical elements for Claim 15 are found in the accused kit.

193. Claim 16 depends on Claim 13 and specifies that the amplified alleles are evaluated by comparing to a "size standard, wherein the size standard is selected from a group of size standards consisting of a DNA marker and a locus specific allelic ladder." As noted above, the Identifiler® Kit comes with a locus specific allelic ladder (paragraphs 105-106) and that a size standard is identified in the "required materials." (paragraph 111). Therefore, I conclude that the technical elements for Claim 16 are found in the accused kit.

Curriculum Vitae

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Education:

Massachusetts Institute of Technology
Postdoctoral Fellow of the Jane Coffin Childs Memorial Fund for Medical Research - 1975-1977
Advisor: Harvey F Lodish

University of California, San Diego - Biology - Ph.D., 1975
Thesis Title: Mutational Analysis of State Specific Enzymes in *Dictyostelium discoideum*
Advisor: William F. Loomis

University of Utah - Biology - B.S., 1970

Awards:

Fellow of The American Academy of Microbiology
National Honor Society
Magna Cum laude - University of Utah
Phi Beta Kappa
USPHS Predoctoral Traineeship, 1070-1975, UCSD
Jane Coffin Childs Memorial Fund for Medical Research
Research Postdoctoral Fellowship
Research Career Development Award, National Institute of Child Health and Human Development 1981-1986

Professional Societies:

Society for Development Biology
American Society for Cell Biology
American Association of Clinical Chemists
American Society for Microbiology
Licensing Executives Society
Association of University Technology Managers

Advisory Committees:

NIH Cell Biology Study Section 1982-1986 (Chairman 1984-1986)
Industrial Liaison Committee - Biotechnology Center - UW- Madison 1985 – 1990
BYU College of Biology and Agriculture National Advisory Committee 1987-1998
Board of Visitors, College of Agriculture and Life Sciences, University of Wisconsin-Madison 2003-2007
Wisconsin Higher Education Business Roundtable – 2007 – present (President)

Professional Experience:

1984-present	Promega Corporation, Vice President-Chief Technical Officer
1985-present	University of Wisconsin – Adjunct Professor of Bacteriology
1981-1985	University of Wisconsin – Associate Professor of Bacteriology
1977-1981	University of Wisconsin – Assistant Professor of Bacteriology
1975-1977	MIT- Postdoctoral Fellow
1970-1975	UCSD – Graduate Student

Teaching Experience:

1979-1985	General Microbiology
1978-1985	Fungal Genetics and Development
1983-1985	Microbial Genetics

Graduate Instruction:

Seven Ph.D. Students
Two M.S. Students
Six Postdoctoral Fellows

Publications

Over 50 published papers in peer review journals and 10 issued patents.

Expert Testimony

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